http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> e kase hiroshi/au
E1            9     KASE HIROMI/AU
E2            3     KASE HIROMITSU/AU
E3          236 --> KASE HIROSHI/AU
E4            1     KASE HIROTOSHI/AU
E5           47     KASE HIROYUKI/AU
E6            1     KASE HISAYUKI/AU
E7            2     KASE HITOMI/AU
E8            1     KASE IKUKO/AU
E9           21     KASE J/AU
E10           1     KASE JASON/AU
E11           3     KASE JASON P/AU
E12           1     KASE JOHANNA/AU

=> s e3
L1          236 "KASE HIROSHI"/AU

=> s l1 and xanthin?
         24194 XANTHIN?
L2           13 L1 AND XANTHIN?

=> d l2 ibib abs ti hit 1-5

L2   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2005:1103616  CAPLUS  Full-text
DOCUMENT NUMBER:         143:373375
TITLE:                   Preventive and/or therapeutic agent for
disease
                         accompanied by chronic muscle/skeleton pain
INVENTOR(S):             Kase, Hiroshi; Takahashi, Isami; Kunori,
                         Shunji; Kobayashi, Minoru; Shiozaki, Shizuo;
                         Shirakura, Shiro
PATENT ASSIGNEE(S):      Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE:                  PCT Int. Appl., 48 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                Japanese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    ----
----
     WO 2005094885         A1    20051013    WO 2005-JP6033
20050330
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
```

NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM,
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL,
PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML,
MR, NE, SN, TD, TG
CA 2561383 A1 20051013 CA 2005-2561383
20050330
EP 1738766 A1 20070103 EP 2005-727903
20050330
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR,
AL, BA,
HR, LV, MK, YU
US 20070149555 A1 20070628 US 2006-594684
20060928
PRIORITY APPLN. INFO.: JP 2004-97422 A
20040330
WO 2005-JP6033 W
20050330
OTHER SOURCE(S): MARPAT 143:373375
AB A preventive and/or therapeutic agent for diseases accompanied by a chronic muscle/skeleton pain contains xanthine derivs. or salts thereof having antagonistic activity against an adenosine A2A receptor. For example, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7- methyl-1H-purine-2,6-dione was tested for pain-relieving effects among rat models with musculoskeletal pain. Formulations for tablets, capsules, and injections were also provided.
TI Preventive and/or therapeutic agent for disease accompanied by chronic
muscle/skeleton pain
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IN Kase, Hiroshi; Takahashi, Isami; Kunori, Shunji; Kobayashi, Minoru; Shiozaki, Shizuo; Shirakura, Shiro
AB A preventive and/or therapeutic agent for diseases accompanied by a chronic muscle/skeleton pain contains xanthine derivs. or salts thereof having antagonistic activity against an adenosine A2A receptor. For example, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7- methyl-1H-purine-2,6-dione was tested for pain-relieving effects among rat models with musculoskeletal pain. Formulations for tablets, capsules, and injections were also provided.
ST xanthine deriv musculoskeletal pain treatment
IT Adenosine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2A, antagonists; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Drug delivery systems
(capsules; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Fatigue, biological
(chronic fatigue syndrome; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Musculoskeletal diseases
(chronic pain; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Lyme disease
(fibromyalgia from; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Muscle, disease
(fibromyalgia; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Muscle, disease
(fibrositis; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Muscle, disease
(generalized tendomyopathy; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Drug delivery systems
(injections; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Muscle, disease
Pain
(myalgia; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Drug delivery systems
(tablets; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Disease, animal
(temporomandibular joint; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Joint, anatomical
(temporomandibular, disease; xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

IT Rheumatic diseases
Rheumatoid arthritis
(xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

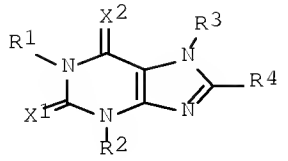
IT 31377-36-3 149744-74-1 861387-30-6 861387-31-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(xanthine derivs. as therapeutic agents for disease accompanied by chronic muscle/skeleton pain)

L2 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:729536 CAPLUS Full-text
DOCUMENT NUMBER: 143:166695
TITLE: Drug for treating migraine
INVENTOR(S): Takeuchi, Megumi; Takayama, Makoto; Shirakura, Shiro;
Kase, Hiroshi

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072739	A1	20050811	WO 2005-JP1634	20050128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2554426	A1	20050811	CA 2005-2554426	20050128
EP 1709967	A1	20061011	EP 2005-704394	20050128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20070161663	A1	20070712	US 2006-587264	20060911
PRIORITY APPLN. INFO.:			JP 2004-19496 A	20040128
			WO 2005-JP1634 W	20050128

OTHER SOURCE(S): MARPAT 143:166695
GI



I

AB Disclosed is a drug for treating migraine which contains, as an active constituent, a xanthine derivative represented by the formula (I) below or a pharmacol. acceptable salt thereof. (In the formulas, I; R1, R2 and R3 may be the same or different and resp. represent a hydrogen atom, a lower alkyl, a lower alkenyl or a lower alkynyl; R4 represents a cycloalkyl, -(CH2)n-R5 or one represented by the above formula (II); and X1 and X2 may be the same or different and resp. represent an oxygen atom or a sulfur atom.).

TI Drug for treating migraine

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN Takeuchi, Megumi; Takayama, Makoto; Shirakura, Shiro; Kase, Hiroshi

AB Disclosed is a drug for treating migraine which contains, as an active constituent, a xanthine derivative represented by the formula (I) below or a pharmacol. acceptable salt thereof. (In the formulas, I; R1, R2 and R3 may be the same or different and resp. represent a hydrogen atom, a lower alkyl, a lower alkenyl or a lower alkynyl; R4 represents a cycloalkyl, -(CH2)n-R5 or one represented by the above formula (II); and X1 and X2 may be the same or different and resp. represent an oxygen atom or a sulfur atom.).

ST xanthine deriv analgesic migraine

IT Drug delivery systems
(capsules; xanthine derivs. for treating migraine)

IT Drug delivery systems
(injections; xanthine derivs. for treating migraine)

IT Headache
(migraine; xanthine derivs. for treating migraine)

IT Drug delivery systems
(tablets; xanthine derivs. for treating migraine)

IT Analgesics
Antimigraine agents
(xanthine derivs. for treating migraine)

IT 69-89-6D, Xanthine, derivs. and salts 31377-36-3 149744-74-1 861387-30-6 861387-31-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(xanthine derivs. for treating migraine)

L2 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:547543 CAPLUS Full-text

DOCUMENT NUMBER: 143:53542

TITLE: Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction

INVENTOR(S): Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo; Kobayashi, Minoru; Toki, Shinichiro; Seno, Naoki; Ikeda, Ken

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056016	A1	20050623	WO 2004-JP18765	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296137	A1	20050623	AU 2004-296137	20041209
CA 2550130	A1	20050623	CA 2004-2550130	20041209
EP 1709966	A1	20061011	EP 2004-807124	20041209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1889959	A	20070103	CN 2004-80036267	20041209
BR 2004017241	A	20070306	BR 2004-17241	20041209
US 20070078148	A1	20070405	US 2006-579829	20060517

MX 2006005965 A 20060809 MX 2006-5965
20060525
KR 2006124615 A 20061205 KR 2006-711123
20060607
IN 2006CN02490 A 20070608 IN 2006-CN2490
20060706
PRIORITY APPLN. INFO.: JP 2003-410432 A
20031209
WO 2004-JP18765 W
20041209
OTHER SOURCE(S): MARPAT 143:53542
AB A preventive and/or therapeutic agent for higher brain dysfunctions which contains as an active ingredient a xanthine derivative represented, for example, by the following formula (I) or a pharmacol. acceptable salt thereof: (I) (II) wherein R1, R2, and R3 are the same or different and each represents hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; R4 represents cycloalkyl, -(CH2)n-R5, or the formula (II) given above; and X1 and X2 are the same or different and each represents oxygen or sulfur. The higher brain dysfunction includes aging brain damage, brain trauma, cerebrovascular disease, memory disorder, thinking disorder, recognition disorder, behavior disorder, learning disorder, etc.
TI Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT
TI Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction
IN Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo; Kobayashi, Minoru; Toki, Shinichiro; Seno, Naoki; Ikeda, Ken

L2 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:99358 CAPLUS Full-text
DOCUMENT NUMBER: 142:162694
TITLE: Medicinal compositions containing adenosine A2A
receptor antagonists and other antidepressants
INVENTOR(S): Kase, Hiroshi; Kobayashi, Minoru; Shiozaki, Shizuo; Mori, Akihisa; Seno, Naoki
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009444	A1	20050203	WO 2004-JP10758	20040722

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,

CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE,
SN, TD, TG
CA 2533117 A1 20050203 CA 2004-2533117
20040722
EP 1655029 A1 20060510 EP 2004-748023
20040722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 20060241102 A1 20061026 US 2006-565239
20060119
NO 2006000958 A 20060425 NO 2006-958
20060227
PRIORITY APPLN. INFO.: JP 2003-201549 A
20030725
WO 2004-JP10758 W
20040722

AB It is intended to provide medicinal compns. and the like useful in treating depression which contain a compound having an antagonism to adenosine A2A receptor (for example, (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purin-2,6-dione) (I) or a pharmacol. acceptable salt thereof together with an antidepressant (for example, a tricyclic antidepressant, a tetracyclic antidepressant, a selective serotonin reuptake inhibitor, a selective noradrenaline reuptake inhibitor, a dopamine reuptake inhibitor, a serotonin/noradrenaline reuptake inhibitor, a monoamine oxidase inhibitor or a serotonin 2 antagonist). The effect of combination of I 0.08 and venlafaxine hydrochloride 5 mg/kg on depression in mice in forced swim test was examined

TI Medicinal compositions containing adenosine A2A receptor antagonists and
other antidepressants

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN Kase, Hiroshi; Kobayashi, Minoru; Shiozaki, Shizuo; Mori, Akihisa; Seno, Naoki

ST adenosine A2A receptor antagonist antidepressant combination; xanthin deriv antidepressant combination

L2 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1080800 CAPLUS Full-text
DOCUMENT NUMBER: 142:33005
TITLE: A method using an adenosine A2A receptor antagonist for treating an anxiety disorder
INVENTOR(S): Kase, Hiroshi; Seno, Naoki; Shiozaki, Shizuo; Kobayashi, Minoru; Kase, Junya
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108137	A1	20041216	WO 2004-JP8486	20040610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004244906	A1	20041216	AU 2004-244906	20040610
CA 2528710	A1	20041216	CA 2004-2528710	20040610
EP 1631294	A1	20060308	EP 2004-746014	20040610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1787821	A	20060614	CN 2004-80012845	

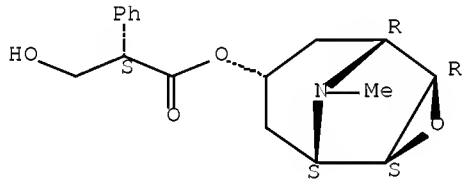
20040610
BR 2004011120 A 20060718 BR 2004-11120
20040610
JP 2006527264 T 20061130 JP 2006-516839
20040610
US 20060281770 A1 20061214 US 2005-553250
20051017
KR 2006037252 A 20060503 KR 2005-721878
20051116
MX 2005013148 A 20060317 MX 2005-13148
20051205
NO 2005005907 A 20051213 NO 2005-5907
20051213
IN 2006CN00077 A 20070629 IN 2006-CN77
20060106
PRIORITY APPLN. INFO.: US 2003-509046P P
20030610
US 2003-532793P P
20031224
WO 2004-JP8486 W
20040610
OTHER SOURCE(S): MARPAT 142:33005
AB Anxiety disorders, such as panic disorder, agoraphobia, obsessive-compulsive disorder, social phobia, post-traumatic stress disorder, generalized anxiety disorder, specific phobia, or the like, are treated by administering an effective amount of at least one adenosine A2A receptor antagonist (e.g. a xanthine derivative) to a patient in need thereof, optionally in combination with an anxiolytic(s) other than the adenosine A2A receptor antagonist.
TI A method using an adenosine A2A receptor antagonist for treating an
anxiety disorder
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IN Kase, Hiroshi; Seno, Naoki; Shiozaki, Shizuo; Kobayashi, Minoru; Kase, Junya
AB Anxiety disorders, such as panic disorder, agoraphobia, obsessive-compulsive disorder, social phobia, post-traumatic stress disorder, generalized anxiety disorder, specific phobia, or the like, are treated by administering an effective amount of at least one adenosine A2A receptor antagonist (e.g. a xanthine derivative) to a patient in need thereof, optionally in combination with an anxiolytic(s) other than the adenosine A2A receptor antagonist.
ST adenosine A2A receptor antagonist anxiolytic; anxiety disorder treatment
adenosine A2A receptor antagonist; xanthine deriv adenosine A2A receptor antagonist anxiolytic
IT 69-89-6D, Xanthine, derivs. 51389-37-8 99331-25-6D, Triazolopyrimidine, derivs. 155270-99-8 262452-04-0 377727-87-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist for treating anxiety disorders)

http://www.cas.org/support/stngen/stndoc/properties.html

```
=> e 51-34-3/rn
E1            1     51-31-0/RN
E2            1     51-33-2/RN
E3            1 --> 51-34-3/RN
E4            1     51-35-4/RN
E5            1     51-36-5/RN
E6            1     51-37-6/RN
E7            1     51-38-7/RN
E8            1     51-39-8/RN
E9            1     51-40-1/RN
E10           1     51-41-2/RN
E11           1     51-42-3/RN
E12           1     51-43-4/RN

=> s e3
L3            1 51-34-3/RN

=> d l3

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   51-34-3  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Benzeneacetic acid, α-(hydroxymethyl)-,
     (1α,2β,4β,5α,7β)-9-methyl-3-oxa-9-
     azatricyclo[3.3.1.02,4]non-7-yl ester, (αS)-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1αH,5αH-Tropan-3α-ol, 6β,7β-epoxy-,
     (-)-tropate (ester) (8CI)
CN   3-Oxa-9-azatricyclo[3.3.1.02,4]nonane, benzeneacetic acid deriv.
CN   Benzeneacetic acid, α-(hydroxymethyl)-,
     9-methyl-3-oxa-9-azatricyclo[3.3.1.02,4]non-7-yl ester,
     [7(S)-(1α,2β,4β,5α,7β)]-
OTHER NAMES:
CN   (-)-Hyoscine
CN   (-)-Scopolamine
CN   6,7-Epoxytropine tropate
CN   6β,7β-Epoxy-3α-tropanyl S-(-)-tropate
CN   9-Methyl-3-oxa-9-azatricyclo[3.3.1.02,4]nonan-7-ol (-)-tropate
CN   Atrochin
CN   Atroquin
CN   Hyoscine
CN   l-Scopolamine
CN   Scop
CN   Scopine (-)-tropate
CN   Scopine tropate
CN   Scopoderm TTS
CN   Scopolamine
CN   SEE
CN   Transcop
CN   Transderm-Scop
CN   Tropic acid ester with scopine
FS   STEREOSEARCH
```

DR 58670-87-4, 14797-94-5, 97991-84-9, 65319-33-7, 28901-63-5, 226562-00-1
MF C17 H21 N O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO,
      CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU,
      DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH,
      IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PHAR,
      PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL,
      USPATOLD, VETU
        (*File contains numerically searchable property data)
    Other Sources: EINECS**
        (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).

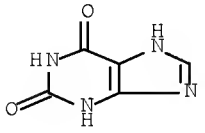


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

          4918 REFERENCES IN FILE CA (1907 TO DATE)
            32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          4923 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e 69-89-6/rn
E1            1     69-81-8/RN
E2            1     69-86-3/RN
E3            1 --> 69-89-6/RN
E4            1     69-90-9/RN
E5            1     69-91-0/RN
E6            1     69-93-2/RN
E7            1     69-96-5/RN
E8            1     690-00-6/RN
E9            1     690-01-7/RN
E10           1     690-02-8/RN
E11           1     690-03-9/RN
E12           1     690-04-0/RN

=> s e3
L4            1 69-89-6/RN

=> d l4
```

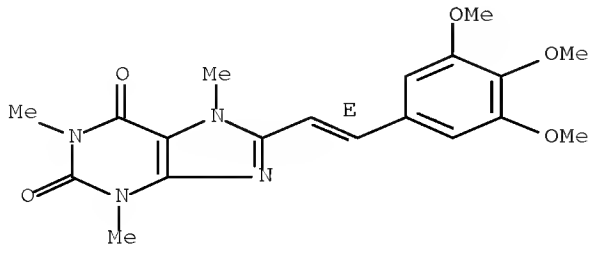
L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 69-89-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1H-Purine-2,6-dione, 3,9-dihydro- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Purine-2,6-dione, 3,7-dihydro- (9CI)
CN Xanthine (8CI)
OTHER NAMES:
CN 1H,3H,7H-Xanthine
CN 1H,3H,9H-Xanthine
CN 1H-Purine-2,6-diol
CN 2,6-Dioxo-1,2,3,6-tetrahydropurine
CN 2,6-Dioxopurine
CN 3,9-Dihydro-1H-purine-2,6-dione
CN 3,9-Dihydropurine-2,6-dione
CN 9H-Purine-2,6(1H,3H)-dione
CN Isoxanthine
CN NSC 14664
CN Pseudoxanthine
CN Purine-2,6(1H,3H)-dione
CN Xan
CN Xanthic oxide
CN Xanthin
DR 16819-86-6, 51953-26-5, 6050-36-8, 6053-41-4, 28522-58-9, 33669-67-9,
42911-15-9
MF C5 H4 N4 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO,
CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN,
CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB,
IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, RTECS*, SPECINFO,
TOXCENTER, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5562 REFERENCES IN FILE CA (1907 TO DATE)
926 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5580 REFERENCES IN FILE CAPLUS (1907 TO DATE)

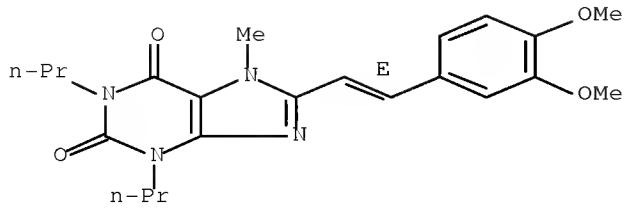
```
=> e 51389-37-8/rn
E1            1     51389-35-6/RN
E2            1     51389-36-7/RN
E3            1 --> 51389-37-8/RN
E4            1     51389-38-9/RN
E5            1     51389-39-0/RN
E6            1     51389-40-3/RN
E7            1     51389-41-4/RN
E8            1     51389-42-5/RN
E9            1     51389-43-6/RN
E10           1     51389-44-7/RN
E11           1     51389-45-8/RN
E12           1     51389-46-9/RN

=> s e3
L5            1 51389-37-8/RN

=> d l5

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   51389-37-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-
     trimethoxyphenyl)ethenyl]-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-
     trimethoxyphenyl)ethenyl]-, (E)-
OTHER NAMES:
CN   KF 18446
CN   trans-8-(3,4,5-Trimethoxystyryl)caffeine
FS   STEREOSEARCH
MF   C19 H22 N4 O5
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, RTECS*, TOXCENTER,
USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
```

14 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e 141807-96-7/rn
E1            1     141807-94-5/RN
E2            1     141807-95-6/RN
E3            1 --> 141807-96-7/RN
E4            1     141807-97-8/RN
E5            1     141807-98-9/RN
E6            1     141807-99-0/RN
E7            1     141808-00-6/RN
E8            1     141808-01-7/RN
E9            1     141808-02-8/RN
E10           1     141808-03-9/RN
E11           1     141808-04-0/RN
E12           1     141808-05-1/RN

=> s e3
L6            1 141807-96-7/RN

=> d l6

L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   141807-96-7  REGISTRY
ED   Entered STN:  12 Jun 1992
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-
dihydro-7-
     methyl-1,3-dipropyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-
dihydro-7-
     methyl-1,3-dipropyl-, (E)-
OTHER NAMES:
CN   KF 17837
CN   KW 17837
FS   STEREOSEARCH
MF   C22 H28 N4 O4
SR   CA
LC   STN Files:   ADISINSIGHT, BEILSTEIN*, BIOSIS, BIOTECHNO, CA,
CAPLUS,
       EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS*, TOXCENTER,
USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```



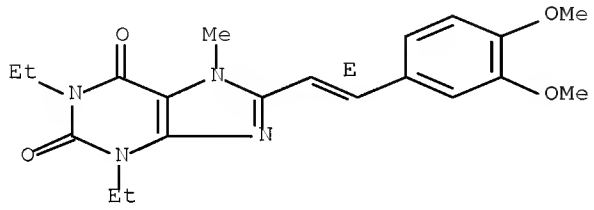
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

55 REFERENCES IN FILE CA (1907 TO DATE)
55 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e 155270-99-8/rn
E1            1     155270-97-6/RN
E2            1     155270-98-7/RN
E3            1 --> 155270-99-8/RN
E4            1     155271-00-4/RN
E5            1     155271-01-5/RN
E6            1     155271-02-6/RN
E7            1     155271-03-7/RN
E8            1     155271-04-8/RN
E9            1     155271-05-9/RN
E10           1     155271-06-0/RN
E11           1     155271-07-1/RN
E12           1     155271-08-2/RN

=> s e3
L7            1 155270-99-8/RN

=> d l7

L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
     dihydro-7-methyl-, (E)-
OTHER NAMES:
CN   Istradefylline
CN   KW 6002
FS   STEREOSEARCH
MF   C20 H24 N4 O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
CA,
       CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,
```

IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE,
TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



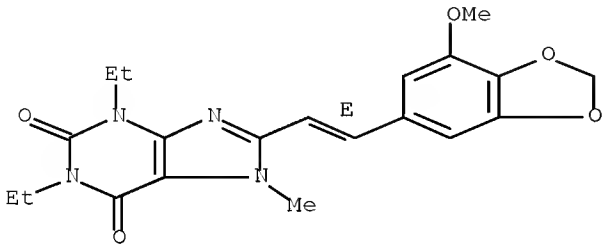
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e 155272-00-7/rn
E1            1     155271-98-0/RN
E2            1     155271-99-1/RN
E3            1 --> 155272-00-7/RN
E4            1     155272-01-8/RN
E5            1     155272-02-9/RN
E6            1     155272-03-0/RN
E7            1     155272-04-1/RN
E8            1     155272-05-2/RN
E9            1     155272-06-3/RN
E10           1     155272-07-4/RN
E11           1     155272-08-5/RN
E12           1     155272-09-6/RN

=> s e3
L8            1 155272-00-7/RN

=> d l8

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155272-00-7  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[(1E)-2-(7-methoxy-
1,3-
     benzodioxol-5-yl)ethenyl]-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-
     benzodioxol-5-yl)ethenyl]-7-methyl-, (E)-
OTHER NAMES:
```

CN (E)-1,3-Diethyl-8-(3,4-methylenedioxy-5-methoxystyryl)-7-methylxanthine
FS STEREOSEARCH
MF C20 H22 N4 O5
SR CA
LC STN Files: CA, CAPLUS, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

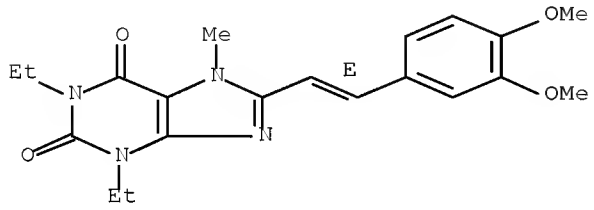
=> e 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl-/cn
E1 1 1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-8-THIOXO-/CN
E2 1 1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-9-METHYL-8-(1,2,6,9-TETRAHY
DRO-9-METHYL-2,6-DIOXO-8H-PURIN-8-YLIDENE)-/CN
E3 0 --> 1H-PURINE-2,6-DIONE, 8-(1E)-2-(3,4-DIMETHOXYPHENYL)ETHENYL
-1,3-DIETHYL-3,7-DIHYDRO-7-METHYL-/CN
E4 1 1H-PURINE-2,6-DIONE, 8-((((2-CHLOROPHENYL)METHYL)AMINO)METHY
L)-3,7-DIHYDRO-1,3-DIMETHYL-/CN
E5 1 1H-PURINE-2,6-DIONE, 8-((((2-CHLOROPHENYL)METHYL)AMINO)METHY
L)-3,9-DIHYDRO-1,3-DIMETHYL-/CN
E6 1 1H-PURINE-2,6-DIONE, 8-(((1,1-DIMETHYLETHYL)AMINO)METHYL)-3,
7-DIHYDRO-1,3,7-TRIMETHYL-/CN
E7 1 1H-PURINE-2,6-DIONE, 8-(((1,1-DIMETHYLETHYL)THIO)METHYL)-3,9
-DIHYDRO-1,3-DIMETHYL-/CN
E8 1 1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3,7-TRIMETHYL-/CN
E9 1 1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-QUINOLINYL)MET
HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-((4-METHYLPHENYL)METHYL

```
                    )-/CN
E10          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
METHYLETHYL)-/CN
E11          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
NAPHTHALENYLMETHYL)-
                    /CN
E12          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(PHENYLMETHYL)-
/CN

=> set expand continuous
SET COMMAND COMPLETED

=> e  1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7- dihydro-7-methyl-, (E)-/cn
E13          1      1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-8-THIOXO-/CN
E14          1      1H-PURINE-2,6-DIONE, 8,9-DIHYDRO-9-METHYL-8-
(1,2,6,9-TETRAHY
                    DRO-9-METHYL-2,6-DIOXO-8H-PURIN-8-YLIDENE)-/CN
E15          0 --> 1H-PURINE-2,6-DIONE, 8-2-(3,4-
DIMETHOXYPHENYL)ETHENYL -1,3-
                    DIETHYL-3,7- DIHYDRO-7-METHYL-, (E)-/CN
E16          1      1H-PURINE-2,6-DIONE, 8-((((2-
CHLOROPHENYL)METHYL)AMINO)METHY
                    L)-3,7-DIHYDRO-1,3-DIMETHYL-/CN
E17          1      1H-PURINE-2,6-DIONE, 8-((((2-
CHLOROPHENYL)METHYL)AMINO)METHY
                    L)-3,9-DIHYDRO-1,3-DIMETHYL-/CN
E18          1      1H-PURINE-2,6-DIONE, 8-(((1,1-
DIMETHYLETHYL)AMINO)METHYL)-3,
                    7-DIHYDRO-1,3,7-TRIMETHYL-/CN
E19          1      1H-PURINE-2,6-DIONE, 8-(((1,1-
DIMETHYLETHYL)THIO)METHYL)-3,9
                    -DIHYDRO-1,3-DIMETHYL-/CN
E20          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3,7-TRIMETHYL-/CN
E21          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-((4-
METHYLPHENYL)METHYL
                    )-/CN
E22          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
METHYLETHYL)-/CN
E23          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(1-
NAPHTHALENYLMETHYL)-
                    /CN
E24          1      1H-PURINE-2,6-DIONE, 8-(((1,2-DIHYDRO-2-OXO-4-
```

```
QUINOLINYL)MET
                    HYL)THIO)-3,7-DIHYDRO-1,3-DIMETHYL-7-(PHENYLMETHYL)-
/CN

=> e Istradefylline/cn
E25           1     ISTONIL/CN
E26           1     ISTOPIRIN/CN
E27           1 --> ISTRADEFYLLINE/CN
E28           1     ISTROEKOL/CN
E29           1     ISTRONA/CN
E30           1     ISU-CCUR/CN
E31           1     ISUBGOL/CN
E32           1     ISUHUMAN/CN
E33           1     ISUMELINE/CN
E34           1     ISUPREL/CN
E35           1     ISUPREN/CN
E36           1     ISURETIN/CN

=> e KW 6002/cn
E37           1     KW 6/CN
E38           2     KW 600/CN
E39           1 --> KW 6002/CN
E40           1     KW 600S/CN
E41           1     KW 6055/CN
E42           1     KW 6066N/CN
E43           1     KW 6151/CN
E44           1     KW 622/CN
E45           1     KW 6629/CN
E46           1     KW 677/CN
E47           1     KW 678/CN
E48           1     KW 7/CN

=> s e27
L9            1 ISTRADEFYLLINE/CN

=> d l9

L9   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
     dihydro-7-methyl-, (E)-
OTHER NAMES:
CN   Istradefylline
CN   KW 6002
FS   STEREOSEARCH
MF   C20 H24 N4 O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
CA,
       CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,
```

IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE,
TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

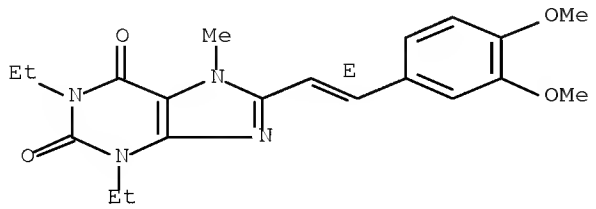
=> s e39
L10 1 "KW 6002"/CN

=> d l10

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 155270-99-8 REGISTRY
ED Entered STN: 24 May 1994
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
3,7-dihydro-7-methyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
dihydro-7-methyl-, (E)-
OTHER NAMES:
CN Istradefylline
CN KW 6002
FS STEREOSEARCH
MF C20 H24 N4 O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
CA,
CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,
IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE,
TOXCENTER, USAN,
USPAT2, USPATFULL

(*File contains numerically searchable property data)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l7 or l9 or l10
           104 L7
           104 L9
           104 L10
L11        104 L7 OR L9 OR L10

=> s l11 and brain, disease/it
        495101 BRAIN/IT
          2040 BRAINS/IT
        495220 BRAIN/IT
                 ((BRAIN OR BRAINS)/IT)
        867672 DISEASE/IT
        105349 DISEASES/IT
        913630 DISEASE/IT
                 ((DISEASE OR DISEASES)/IT)
         71978 BRAIN, DISEASE/IT
                 ((BRAIN(W)DISEASE)/IT)
L12          6 L11 AND BRAIN, DISEASE/IT

=> s (l7 or l9 or l10)
           104 L7
           104 L9
           104 L10
L13        104 (L7 OR L9 OR L10)

=> s l13 and learning disorders/it
         18467 LEARNING/IT
             4 LEARNINGS/IT
         18470 LEARNING/IT
```

```
                ((LEARNING OR LEARNINGS)/IT)
        145760 DISORDERS/IT
          1263 LEARNING DISORDERS/IT
                ((LEARNING(W)DISORDERS)/IT)
L14          1 L13 AND LEARNING DISORDERS/IT

=> s l13 and memory disorders/it
        104513 MEMORY/IT
          1779 MEMORIES/IT
        104686 MEMORY/IT
                ((MEMORY OR MEMORIES)/IT)
        145760 DISORDERS/IT
          2980 MEMORY DISORDERS/IT
                ((MEMORY(W)DISORDERS)/IT)
L15          1 L13 AND MEMORY DISORDERS/IT

=> s l13 and mental and behavioral disorders/it
         66412 MENTAL
             5 MENTALS
         66416 MENTAL
                (MENTAL OR MENTALS)
         31717 BEHAVIORAL/IT
         31717 BEHAVIORAL/IT
                ((BEHAVIORAL OR BEHAVIOURAL)/IT)
        145760 DISORDERS/IT
         20949 BEHAVIORAL DISORDERS/IT
                ((BEHAVIORAL(W)DISORDERS)/IT)
L16          7 L13 AND MENTAL AND BEHAVIORAL DISORDERS/IT

=> s l12 and (py<2003 or ay<2003 or pry<2003)
      22983605 PY<2003
       4504987 AY<2003
       3974028 PRY<2003
L17          2 L12 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> s l16 and (py<2003 or ay<2003 or pry<2003)
      22983605 PY<2003
       4504987 AY<2003
       3974028 PRY<2003
L18          2 L16 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d l17 ibib abs ti hit 1-2

L17  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:566535  CAPLUS  Full-text
DOCUMENT NUMBER:         141:99728
TITLE:                   A method using
                         (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-
                         methylxanthine for treating behavioral
disorders
INVENTOR(S):             Shiozaki, Shizuo; Shimada, Junichi; Kase,
Hiroshi;
                         Shindo, Mayumi
PATENT ASSIGNEE(S):      Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE:                  PCT Int. Appl., 24 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
```

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	20031224 <--
WO 2004058139	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511779	A1	20040715	CA 2003-2511779	20031224 <--
AU 2003299432	A1	20040722	AU 2003-299432	20031224 <--
EP 1581163	A2	20051005	EP 2003-799729	20031224 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017772	A	20051122	BR 2003-17772	20031224 <--
CN 1732005	A	20060208	CN 2003-80107517	20031224 <--
JP 2006513207	T	20060420	JP 2004-563530	20031224 <--
ZA 2005004955	A	20060426	ZA 2005-4955	20050617 <--
MX 2005006860	A	20050818	MX 2005-6860	20050622 <--
US 20060069107	A1	20060330	US 2005-539574	20050728 <--
US 20090023755	A1	20090122	US 2008-239955	20080929 <--
PRIORITY APPLN. INFO.:			US 2002-509039P P	20021227 <--
			WO 2003-IB6455 W	20031224
			US 2005-539574 A1	

20050728
AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also be used for Tic/Tourette's disorder.
TI A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine
for treating behavioral disorders
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
PRAI US 2002-509039P P 20021227 <--
WO 2003-IB6455 W 20031224
US 2005-539574 A1 20050728
IT Brain, disease
(Gilles de la Tourette syndrome, tic/Tourette's disorder; xanthine
derivative for treatment of behavioral disorders)
IT 155270-99-8
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)

L17 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:644563 CAPLUS Full-text
DOCUMENT NUMBER: 130:33316
TITLE: Adenosine A2A receptors modify motor function in
MPTP-treated common marmosets
AUTHOR(S): Kanda, Tomoyuki; Tashiro, Tomomi; Kuwana, Yoshihisa;
Jenner, Peter
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo
Co Ltd, Shizuoka, 411-8731, Japan
SOURCE: NeuroReport (1998), 9(12), 2857-2860
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both adenosine A1 and A2 receptor populations are located in the striatum and can modify locomotor activity, and they may form a therapeutic target for Parkinson's disease (PD). Administration of the selective adenosine A2A antagonist (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7- dihydro-1H-purine-2,6-dione (KW-6002) to MPTP-treated common marmosets increased locomotor activity. In contrast, administration of the selective A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxantine (DPCPX) had no effect on locomotion. Administration of the adenosine A2A receptor agonist 2-[p-[2-(2-aminoethylamino) carbonylethyl] phenethyl amino]-5'-N-ethylcarboxamidoadenosine (APEC) dose dependently suppressed basal locomotor activity. A minimally ED of APEC (0.62 mg/kg, i.p) completely reversed the increase in

locomotor activity produced by administration of KW-6002. The adenosine A2A receptor appears to be an important target for the treatment of basal ganglia disorders, particularly PD.

TI Adenosine A2A receptors modify motor function in MPTP-treated common marmosets

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO NeuroReport (1998), 9(12), 2857-2860
CODEN: NERPEZ; ISSN: 0959-4965

IT Brain, disease
(basal ganglion; adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

IT 155270-99-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

=> d l18 ibib abs ti hit 1-2

L18 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:463565 CAPLUS Full-text
DOCUMENT NUMBER: 144:460860
TITLE: Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders
INVENTOR(S): Grzelak, Michael; Hunter, John; Pond, Annamarie; Varty, Geoffrey
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 738,906.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060106040	A1	20060518	US 2005-234644	20050923 <--
US 20040138235	A1	20040715	US 2003-738906	20031217 <--
US 7414058	B2	20080819		

CA 2510655 A1 20050519 CA 2003-2510655
20031217 <--
AU 2003304527 A1 20050526 AU 2003-304527
20031217 <--
EP 1578409 A1 20050928 EP 2003-818838
20031217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003017436 A 20051116 BR 2003-17436
20031217 <--
JP 2006514697 T 20060511 JP 2005-510511
20031217 <--
NZ 540493 A 20080430 NZ 2003-540493
20031217 <--
CN 101310724 A 20081126 CN 2008-10136154
20031217 <--
MX 2005006790 A 20050908 MX 2005-6790
20050620 <--
US 20060128694 A1 20060615 US 2005-249796
20051013 <--
AU 2006294919 A1 20070405 AU 2006-294919
20060921
CA 2623040 A1 20070405 CA 2006-2623040
20060921
WO 2007038212 A1 20070405 WO 2006-US36864
20060921
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG,
MK, MN,
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR,
TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,
BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,
BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY,
KG, KZ, MD, RU, TJ, TM
EP 1940408 A1 20080709 EP 2006-815125
20060921
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK,
TR, AL,
BA, HR, MK, RS
JP 2009508967 T 20090305 JP 2008-532393

20060921
MX 2008004006 A 20080410 MX 2008-4006
20080324
CN 101312731 A 20081126 CN 2006-80043146
20080519
PRIORITY APPLN. INFO.: US 2002-435321P P
20021219 <--
US 2003-738906 A2
20031217
CN 2003-80107087 A3
20031217
WO 2003-US40456 W
20031217
US 2005-234644 A2
20050923
WO 2006-US36864 W
20060921
OTHER SOURCE(S): MARPAT 144:460860
AB The invention discloses a method for the treatment or prevention of extrapyramidal syndrome (EPS), dystonia, restless legs syndrome (RLS) or periodic leg movement in sleep (PLMS), comprising the administration of an adenosine A2a receptor antagonist, alone or in combination with other agents useful for treating EPS, dystonia, RLS or PLMS.
TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal
syndrome and other movement disorders
PRAI US 2002-435321P P 20021219 <--
US 2003-738906 A2 20031217
CN 2003-80107087 A3 20031217
WO 2003-US40456 W 20031217
US 2005-234644 A2 20050923
WO 2006-US36864 W 20060921
IT Mental and behavioral disorders
(depression, dystonia from antidepressant use; adenosine A2a receptor
antagonists for treatment of extrapyramidal syndrome and other movement
disorders)
IT Mental and behavioral disorders
(psychosis, extrapyramidal syndrome from typical or atypical antipsychotic use; adenosine A2a receptor antagonists for treatment of
extrapyramidal syndrome and other movement disorders)
IT 59-92-7, Levodopa, biological studies 322-35-0, Benserazide
7439-89-6D, Iron, salts 12794-10-4D, Benzodiazepine, derivs.
28860-95-9, Carbidopa 155270-99-8 377727-26-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2a receptor antagonists for treatment of extrapyramidal
syndrome and other movement disorders)

L18 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:566535 CAPLUS Full-text
DOCUMENT NUMBER: 141:99728
TITLE: A method using

(E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine for treating behavioral disorders

INVENTOR(S): Shiozaki, Shizuo; Shimada, Junichi; Kase, Hiroshi; Shindo, Mayumi

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

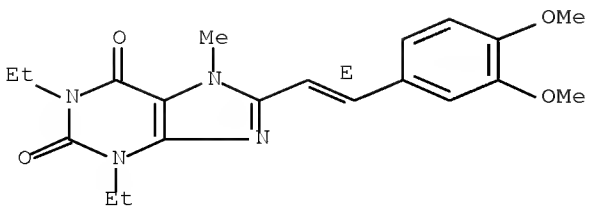
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	20031224 <--
WO 2004058139	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511779	A1	20040715	CA 2003-2511779	20031224 <--
AU 2003299432	A1	20040722	AU 2003-299432	20031224 <--
EP 1581163	A2	20051005	EP 2003-799729	20031224 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017772	A	20051122	BR 2003-17772	20031224 <--
CN 1732005	A	20060208	CN 2003-80107517	20031224 <--
JP 2006513207	T	20060420	JP 2004-563530	20031224 <--
ZA 2005004955	A	20060426	ZA 2005-4955	20050617 <--
MX 2005006860	A	20050818	MX 2005-6860	

20050622 <--
US 20060069107 A1 20060330 US 2005-539574
20050728 <--
US 20090023755 A1 20090122 US 2008-239955
20080929 <--
PRIORITY APPLN. INFO.: US 2002-509039P P
20021227 <--
WO 2003-IB6455 W
20031224
US 2005-539574 A1
20050728
AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also be used for Tic/Tourette's disorder.
TI A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine
for treating behavioral disorders
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
PRAI US 2002-509039P P 20021227 <--
WO 2003-IB6455 W 20031224
US 2005-539574 A1 20050728
IT Brain, disease
(Gilles de la Tourette syndrome, tic/Tourette's disorder; xanthine
derivative for treatment of behavioral disorders)
IT Mental and behavioral disorders
(attention deficit hyperactivity disorder; xanthine derivative for
treatment of behavioral disorders)
IT Drug delivery systems
(capsules; xanthine derivative for treatment of behavioral disorders)
IT Drug delivery systems
(injections; xanthine derivative for treatment of behavioral disorders)
IT Behavior
(locomotor; xanthine derivative for treatment of behavioral disorders)
IT Drug delivery systems
(tablets; xanthine derivative for treatment of behavioral disorders)
IT Central nervous system
(tic/Tourette's disorder; xanthine derivative for treatment of behavioral disorders)
IT Mental and behavioral disorders
(xanthine derivative for treatment of behavioral disorders)
IT 155270-99-8
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)

(xanthine derivative for treatment of behavioral disorders)

http://www.cas.org/support/stngen/stndoc/properties.html

```
=> e 155270-99-8/rn
E1            1     155270-97-6/RN
E2            1     155270-98-7/RN
E3            1 --> 155270-99-8/RN
E4            1     155271-00-4/RN
E5            1     155271-01-5/RN
E6            1     155271-02-6/RN
E7            1     155271-03-7/RN
E8            1     155271-04-8/RN
E9            1     155271-05-9/RN
E10           1     155271-06-0/RN
E11           1     155271-07-1/RN
E12           1     155271-08-2/RN

=> set expand continuous
SET COMMAND COMPLETED

=> s e3
L1            1 155270-99-8/RN

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
     dihydro-7-methyl-, (E)-
OTHER NAMES:
CN   Istradefylline
CN   KW 6002
FS   STEREOSEARCH
MF   C20 H24 N4 O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
CA,
       CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,
IMSRESEARCH,
       IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE,
TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```



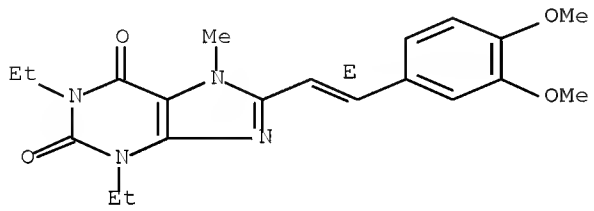
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e istradefylline/cn
E13             1     ISTONIL/CN
E14             1     ISTOPIRIN/CN
E15             1 --> ISTRADEFYLLINE/CN
E16             1     ISTROEKOL/CN
E17             1     ISTRONA/CN
E18             1     ISU-CCUR/CN
E19             1     ISUBGOL/CN
E20             1     ISUHUMAN/CN
E21             1     ISUMELINE/CN
E22             1     ISUPREL/CN
E23             1     ISUPREN/CN
E24             1     ISURETIN/CN

=> s e15
L2              1 ISTRADEFYLLINE/CN

=> d l2

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
     dihydro-7-methyl-, (E)-
OTHER NAMES:
CN   Istradefylline
CN   KW 6002
FS   STEREOSEARCH
MF   C20 H24 N4 O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
CA,
```

CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



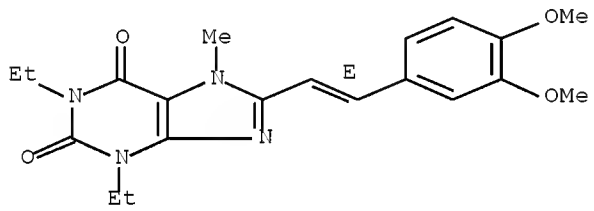
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e kw 6002/cn
E25             1     KW 6/CN
E26             2     KW 600/CN
E27             1 --> KW 6002/CN
E28             1     KW 600S/CN
E29             1     KW 6055/CN
E30             1     KW 6066N/CN
E31             1     KW 6151/CN
E32             1     KW 622/CN
E33             1     KW 6629/CN
E34             1     KW 677/CN
E35             1     KW 678/CN
E36             1     KW 7/CN

=> s e27
L3              1 "KW 6002"/CN

=> d l3

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
```

dihydro-7-methyl-, (E)-
OTHER NAMES:
CN Istradefylline
CN KW 6002
FS STEREOSEARCH
MF C20 H24 N4 O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,
CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (l1 or l2 or l3) and (brain or memory or ?cognition or apraxia or learning)

```
          104 L1
          104 L2
          104 L3
       608007 BRAIN
        28279 BRAINS
       611310 BRAIN
                (BRAIN OR BRAINS)
       179119 MEMORY
         7454 MEMORIES
       181248 MEMORY
                (MEMORY OR MEMORIES)
       165227 ?COGNITION
          145 APRAXIA
            1 APRAXIAS
          145 APRAXIA
                (APRAXIA OR APRAXIAS)
        42736 LEARNING
          105 LEARNINGS
        42830 LEARNING
```

```
                (LEARNING OR LEARNINGS)
L4          27 (L1 OR L2 OR L3) AND (BRAIN OR MEMORY OR ?COGNITION OR
APRAXIA
               OR LEARNING)

=> s l4 and (py<2003 or ay<2003 or pry<2003)
      22983605 PY<2003
       4504987 AY<2003
       3974028 PRY<2003
L5            8 L4 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d l5 ibib abs ti hit 1-8

L5   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2004:566535  CAPLUS  Full-text
DOCUMENT NUMBER:          141:99728
TITLE:                    A method using
                          (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-
                          methylxanthine for treating behavioral
disorders
INVENTOR(S):              Shiozaki, Shizuo; Shimada, Junichi; Kase,
Hiroshi;
                          Shindo, Mayumi
PATENT ASSIGNEE(S):       Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE:                   PCT Int. Appl., 24 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   ----
----
     WO 2004058139         A2    20040715    WO 2003-IB6455
20031224 <--
     WO 2004058139         A3    20041104
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NI, NO,
             NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SY, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
     CA 2511779            A1    20040715    CA 2003-2511779
```

20031224 <--
AU 2003299432 A1 20040722 AU 2003-299432
20031224 <--
EP 1581163 A2 20051005 EP 2003-799729
20031224 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003017772 A 20051122 BR 2003-17772
20031224 <--
CN 1732005 A 20060208 CN 2003-80107517
20031224 <--
JP 2006513207 T 20060420 JP 2004-563530
20031224 <--
ZA 2005004955 A 20060426 ZA 2005-4955
20050617 <--
MX 2005006860 A 20050818 MX 2005-6860
20050622 <--
US 20060069107 A1 20060330 US 2005-539574
20050728 <--
US 20090023755 A1 20090122 US 2008-239955
20080929 <--
PRIORITY APPLN. INFO.: US 2002-509039P P
20021227 <--
WO 2003-IB6455 W
20031224
US 2005-539574 A1
20050728
AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also be used for Tic/Tourette's disorder.
TI A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine
for treating behavioral disorders
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
PRAI US 2002-509039P P 20021227 <--
WO 2003-IB6455 W 20031224
US 2005-539574 A1 20050728
IT Brain, disease
(Gilles de la Tourette syndrome, tic/Tourette's disorder; xanthine
derivative for treatment of behavioral disorders)
IT 155270-99-8
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:610271 CAPLUS Full-text
DOCUMENT NUMBER: 139:143978

TITLE: Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine agonist therapy-associated movement disorders

INVENTOR(S): Kase, Hiroshi; Mori, Akihisa; Waki, Yutaka; Ohsawa, Yutaka; Karasawa, Akira; Kuwana, Yoshitoshi

PATENT ASSIGNEE(S): Japan

SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063876	A2	20030807	WO 2003-US2658	20030128 <--
WO 2003063876	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473864	A1	20030807	CA 2003-2473864	20030128 <--
US 20040198753	A1	20041007	US 2003-353240	20030128 <--
EP 1469855	A2	20041027	EP 2003-705971	20030128 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003006919	A	20041109	BR 2003-6919	20030128 <--
CN 1646132	A	20050727	CN 2003-802847	20030128 <--
JP 2005523898	T	20050811	JP 2003-563566	20030128 <--

AU 2003207734 B2 20080221 AU 2003-207734
20030128 <--
MX 2004007299 A 20041029 MX 2004-7299
20040728 <--
US 20060148827 A1 20060706 US 2006-326516
20060106 <--
US 20060178379 A1 20060810 US 2006-326414
20060106 <--
AU 2008200611 A1 20080306 AU 2008-200611
20080208
PRIORITY APPLN. INFO.: US 2002-352413P P
20020128 <--
AU 2003-207734 A3
20030128
US 2003-353240 A3
20030128
WO 2003-US2658 W
20030128
OTHER SOURCE(S): MARPAT 139:143978
AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e., L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.
TI Methods using adenosine A2A receptor antagonists for treating Parkinson's
disease patients suffering from L-DOPA/dopamine agonist therapy-associated
movement disorders
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
PRAI US 2002-352413P P 20020128 <--
AU 2003-207734 A3 20030128
US 2003-353240 A3 20030128
WO 2003-US2658 W 20030128
IT Brain
(substantia nigra, pars reticulata; adenosine A2a antagonist for
treating Parkinson's disease patients with L-DOPA/dopamine agonist
therapy-associated motor complications)

IT 69-89-6D, Xanthine, derivs. 322-35-0, Benserazide 155270-99-8, KW 6002
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2a antagonist for treating Parkinson's disease patients
with L-DOPA/dopamine agonist therapy-associated motor complications)

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:793451 CAPLUS Full-text
DOCUMENT NUMBER: 137:289033
TITLE: Adenosine A2A receptor antagonists combined with
neurotrophic activity compounds in the treatment of
Parkinson's disease
INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen, Karin
Sandager
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080957	A1	20021017	WO 2002-DK228	20020404 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440196	A1	20021017	CA 2002-2440196	20020404 <--
AU 2002338309	A1	20021021	AU 2002-338309	20020404 <--
EP 1379269	A1	20040114	EP 2002-759761	20020404 <--
EP 1379269	B1	20090304		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004529916 T 20040930 JP 2002-578996 20020404 <--
US 20040097540 A1 20040520 US 2003-473809 20031002 <--
US 7160899 B2 20070109
MX 2003009185 A 20040217 MX 2003-9185 20031008 <--
PRIORITY APPLN. INFO.: DK 2001-583 A 20010409 <--
WO 2002-DK228 W 20020404 <--
AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H- pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3- dione-3-oxime; GDNF; Neublastin; and pharmaceutically acceptable salts thereof.
TI Adenosine A2A receptor antagonists combined with neurotrophic activity
compounds in the treatment of Parkinson's disease
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
PI WO 2002080957 A1 20021017

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002080957	A1	20021017	WO 2002-DK228	20020404 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2440196 A1 20021017 CA 2002-2440196 20020404 <--

AU 2002338309 A1 20021021 AU 2002-338309
20020404 <--
EP 1379269 A1 20040114 EP 2002-759761
20020404 <--
EP 1379269 B1 20090304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004529916 T 20040930 JP 2002-578996
20020404 <--
US 20040097540 A1 20040520 US 2003-473809
20031002 <--
US 7160899 B2 20070109
MX 2003009185 A 20040217 MX 2003-9185
20031008 <--
PRAI DK 2001-583 A 20010409 <--
WO 2002-DK228 W 20020404 <--
IT Brain
(nigrostriatal dopaminergic tract; adenosine A2A receptor
antagonists
combined with neurotrophic compds. in treatment of Parkinson's
disease)
IT 14114-46-6, DMPX 104615-18-1, CGS-15943 139180-30-6, ZM-241385
141807-96-7, KF-17837 155270-99-8, KW-6002 160098-96-4,
SCH-58261 160753-58-2 309711-72-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(adenosine A2A receptor antagonists combined with neurotrophic
compds.
in treatment of Parkinson's disease)

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:787693 CAPLUS Full-text
DOCUMENT NUMBER: 138:314421
TITLE: Distribution of adenosine A2A receptor
antagonist
KW-6002 and its effect on gene expression in
the rat
brain
AUTHOR(S): Aoyama, Shiro; Koga, Kumiko; Mori, Akihisa;
Miyaji,
Hiromasa; Sekine, Susumu; Kase, Hiroshi;
Uchimura,
Tatsuo; Kobayashi, Hiroyuki; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Res. Inst., Kyowa Hakko Kogyo
Co. Ltd.,
Sunto-gun, Shizuoka, 411-8731, Japan
SOURCE: Brain Research (2002), 953(1,2), 119-125
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-
1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-
purine- 2,6-dione], possesses antiparkinsonian activities in
rodent and primate models. In the present study, the authors
investigated the distribution of [14C]KW-6002 in forebrain after

oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [14C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the brain. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [14C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-containing neurons but not striatonigral substance P-containing neurons.

TI Distribution of adenosine A2A receptor antagonist KW-6002 and its effect
on gene expression in the rat brain

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Distribution of adenosine A2A receptor antagonist KW-6002 and its effect
on gene expression in the rat brain

SO Brain Research (2002), 953(1,2), 119-125
CODEN: BRREAP; ISSN: 0006-8993

AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine- 2,6-dione], possesses antiparkinsonian activities in rodent and primate models. In the present study, the authors investigated the distribution of [14C]KW-6002 in forebrain after oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [14C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the brain. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [14C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-

containing neurons but not striatonigral substance P-containing neurons.

IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2A, antagonist; distribution of adenosine A2A receptor antagonist
KW-6002 and its effect on gene expression in rat brain)

IT Brain
(corpus striatum; distribution of adenosine A2A receptor antagonist
KW-6002 and its effect on gene expression in rat brain)

IT Antiparkinsonian agents
Parkinson's disease
(distribution of adenosine A2A receptor antagonist KW-6002 and its
effect on gene expression in rat brain)

IT Brain
(forebrain; distribution of adenosine A2A receptor antagonist KW-6002
and its effect on gene expression in rat brain)

IT Tachykinins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepro-; distribution of adenosine A2A receptor antagonist KW-6002 and
its effect on gene expression in rat brain)

IT 93443-35-7, Preproenkephalin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of adenosine A2A receptor antagonist KW-6002 and its
effect on gene expression in rat brain)

IT 155270-99-8, KW-6002
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(distribution of adenosine A2A receptor antagonist KW-6002 and its
effect on gene expression in rat brain)

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:90903 CAPLUS Full-text
DOCUMENT NUMBER: 136:277364
TITLE: Neuroprotection by adenosine A2A receptor blockade in
experimental models of Parkinson's disease
AUTHOR(S): Ikeda, Ken; Kurokawa, Masako; Aoyama, Shiro; Kuwana,
Yoshihisa
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo
Co., Ltd., Shizuoka, 411-8731, Japan
SOURCE: Journal of Neurochemistry (2002), 80(2), 262-270
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenosine A2A receptors are abundant in the caudate-putamen and involved in the motor control in several species. In MPTP-treated

monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the present study, a significant neuroprotective effect of A2A receptor antagonists is shown in exptl. models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The neuroprotective property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically neuroprotective activities.

TI Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Journal of Neurochemistry (2002), 80(2), 262-270
CODEN: JONRA9; ISSN: 0022-3042

IT Brain
(corpus striatum; adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

IT Brain
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

IT 155270-99-8, KW-6002
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:864519 CAPLUS Full-text

DOCUMENT NUMBER: 136:129190

TITLE: Solubilization and immunoprecipitation of rat striatal adenosine A2A receptors

AUTHOR(S): Harvey, Victoria; Jones, Julie; Misra, Anil; Knight, Antony R.; Quirk, Kathleen

CORPORATE SOURCE: Department of Molecular Pharmacology, Vernalis Research Ltd., Winnersh, Wokingham, RG41 5UA, UK

SOURCE: European Journal of Pharmacology (2001), 431(2), 171-177
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, the authors have sought to solubilize adenosine A2A receptors from rat striatal membranes using a variety of different detergents. Of the detergents tested, 1% CHAPS yielded optimal conditions for solubilization (in the presence of 3 mg/mL protein, 44% of receptor was solubilized, 50% of total protein was solubilized). An antipeptide antibody was raised against a 15 amino-acid sequence within the predicted third intracellular loop region of the human and rat adenosine A2A receptor. The antibody was coupled to protein A immobilized on sepharose CL-4B and used to immunoppt. adenosine A2A receptors from solubilized rat striatal prepns. Radioligand-binding studies were performed using the selective adenosine A2 antagonist [3H]ZM 241385. Using [3H]ZM 241385, the pharmacol. of immunopptd. adenosine A2A receptors was composed to striatal membrane bound adenosine A2A receptors and detergent solubilized adenosine A2A receptors. [H]ZM 241385 labeled a single saturable binding site with high affinity in all three prepns. (membrane bound Kd 2.7 nM; solubilized Kd 1.9 nM; immunopptd. Kd 2.2 nM). Addnl., all three assays confirmed a rank order of potency for displacers consistent with adenosine A2A receptor pharmacol.: ZM 241385 > KW 6002 > CGS 21680 > DPCPX. The authors conclude that they have solubilized and immunopptd. adenosine A2A receptors from rat striatum and that their pharmacol. is consistent with native striatal adenosine A2A receptors.

TI Solubilization and immunoprecipitation of rat striatal adenosine A2A receptors

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO European Journal of Pharmacology (2001), 431(2), 171-177
CODEN: EJPHAZ; ISSN: 0014-2999

IT Brain
(corpus striatum; adenosine A2A receptors of rat striatum solubilization and immunopptn.)

IT 102146-07-6, DPCPX 120225-54-9, CGS 21680 155270-99-8, KW 6002
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine A2A receptors of rat striatum solubilization and immunopptn.)

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:637359 CAPLUS Full-text
DOCUMENT NUMBER: 134:430
TITLE: Systemic administration of adenosine A2A receptor antagonist reverses increased GABA release in the globus pallidus of unilateral 6-hydroxydopamine-lesioned rats: a microdialysis study

AUTHOR(S): Ochi, M.; Koga, K.; Kurokawa, M.; Kase, H.; Nakamura,
J.; Kuwana, Y.
CORPORATE SOURCE: Kyowa Hakko Kogyo, Pharmaceutical Research Institute,
Nagaizumi, Sunto, Shizuoka, 411-8731, Japan
SOURCE: Neuroscience (Oxford) (2000), 100(1), 53-62
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of adenosine A2A receptor antagonists to exhibit antiparkinsonian activity has recently been reported, but the mechanisms of action are still unknown. Since A2A receptors have been localized to GABAergic striatopallidal neurons, it is probable that these antagonists affect the activity of these neurons. In the present study, extracellular GABA basal levels were increased in the ipsilateral striatum and globus pallidus following a unilateral 6-hydroxydopamine lesion of the nigrostriatal pathway. The A2A receptor-selective antagonist KW-6002 (3 mg/kg, p.o.) caused a marked and sustained decrease of extracellular GABA levels in the globus pallidus of the 6-hydroxydopamine-lesioned rats, whereas no changes in GABA levels were observed in the globus pallidus of the non-lesioned rats. Microinjection of the A2A receptor agonist CGS21680 (0.005-0.5 μg) into the striatum of non-lesioned animals increased GABA concns. in the globus pallidus, which was abolished by the voltage-dependent Na+ channel blocker tetrodotoxin (1 μmol/l) delivered locally to the globus pallidus via the dialysis membrane. Furthermore, intrapallidal infusion of CGS21680 (10 μmol/l) also increased GABA levels in the globus pallidus. These data indicate that GABA release from striatopallidal neurons is regulated through A2A receptors in both the striatum and globus pallidus. The reversal of the 6-hydroxydopamine-induced increase in pallidal GABA levels by KW-6002 suggests that the antiparkinsonian effects of A2A receptor antagonists occur on the striatopallidal neurons.
TI Systemic administration of adenosine A2A receptor antagonist reverses
increased GABA release in the globus pallidus of unilateral 6-hydroxydopamine-lesioned rats: a microdialysis study
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Neuroscience (Oxford) (2000), 100(1), 53-62
CODEN: NRSCDN; ISSN: 0306-4522
IT Brain
(corpus striatum, GABAergic system; adenosine A2A receptor antagonist
reverses increased GABA release in globus pallidus of unilateral
6-hydroxydopamine-lesioned rats)
IT Brain
(globus pallidus; adenosine A2A receptor antagonist reverses increased
GABA release in globus pallidus of unilateral

6-hydroxydopamine-lesioned rats)
IT Brain
(striatopallidonigral tract; adenosine A2A receptor antagonist reverses
increased GABA release in globus pallidus of unilateral
6-hydroxydopamine-lesioned rats)
IT 155270-99-8, KW-6002
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(adenosine A2A receptor antagonist reverses increased GABA release in
globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:644563 CAPLUS Full-text
DOCUMENT NUMBER: 130:33316
TITLE: Adenosine A2A receptors modify motor function in
MPTP-treated common marmosets
AUTHOR(S): Kanda, Tomoyuki; Tashiro, Tomomi; Kuwana, Yoshihisa;
Jenner, Peter
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo
Co Ltd, Shizuoka, 411-8731, Japan
SOURCE: NeuroReport (1998), 9(12), 2857-2860
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both adenosine A1 and A2 receptor populations are located in the striatum and can modify locomotor activity, and they may form a therapeutic target for Parkinson's disease (PD). Administration of the selective adenosine A2A antagonist (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7- dihydro-1H-purine-2,6-dione (KW-6002) to MPTP-treated common marmosets increased locomotor activity. In contrast, administration of the selective A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxantine (DPCPX) had no effect on locomotion. Administration of the adenosine A2A receptor agonist 2-[p-[2-(2-aminoethylamino) carbonylethyl] phenethyl amino]-5'-N-ethylcarboxamidoadenosine (APEC) dose dependently suppressed basal locomotor activity. A minimally ED of APEC (0.62 mg/kg, i.p) completely reversed the increase in locomotor activity produced by administration of KW-6002. The adenosine A2A receptor appears to be an important target for the treatment of basal ganglia disorders, particularly PD.
TI Adenosine A2A receptors modify motor function in MPTP-treated common
marmosets
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO NeuroReport (1998), 9(12), 2857-2860

```
     CODEN: NERPEZ; ISSN: 0959-4965
IT   Brain, disease
        (basal ganglion; adenosine A2A receptors modify motor function
in
        MPTP-treated common marmoset Parkinsonism model)
IT   Brain
        (corpus striatum; adenosine A2A receptors modify motor function
in
        MPTP-treated common marmoset Parkinsonism model)
IT   155270-99-8
     RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
study); USES
     (Uses)
        (adenosine A2A receptors modify motor function in MPTP-treated
common
        marmoset Parkinsonism model)


=> s (l1 or l2 or l3) and  (memory or ?cognition or apraxia or
learning)
           104 L1
           104 L2
           104 L3
        179119 MEMORY
          7454 MEMORIES
        181248 MEMORY
                 (MEMORY OR MEMORIES)
        165227 ?COGNITION
           145 APRAXIA
             1 APRAXIAS
           145 APRAXIA
                 (APRAXIA OR APRAXIAS)
         42736 LEARNING
           105 LEARNINGS
         42830 LEARNING
                 (LEARNING OR LEARNINGS)
L6           3 (L1 OR L2 OR L3) AND  (MEMORY OR ?COGNITION OR APRAXIA
OR LEARNI
               NG)

=> d l6 ibib abs ti hit 1-3

L6   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2008:446836  CAPLUS  Full-text
DOCUMENT NUMBER:         149:462747
TITLE:                   Adenosine A2A receptor blockade prevents
                         memory dysfunction caused by β-amyloid
                         peptides but not by scopolamine or MK-801
AUTHOR(S):               Cunha, Geanne M. A.; Canas, Paula M.; Melo,
Carolina
                         S.; Hockemeyer, Joerg; Mueller, Christa E.;
Oliveira,
                         Catarina R.; Cunha, Rodrigo A.
CORPORATE SOURCE:        Center for Neuroscience of Coimbra, Institute
of
```

Biochemistry, Faculty of Medicine, University of
Coimbra, Coimbra, 3004-504, Port.
SOURCE: Experimental Neurology (2008), 210(2), 776-781
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adenosine A2A receptor antagonists alleviate memory deficits caused by aging or by administration of β-amyloid peptides in rodents, which is in accordance with the beneficial effects of caffeine consumption (an adenosine receptor antagonist) on memory performance in aged individuals and in preventing Alzheimer's disease. We now tested if A2A receptor blockade affords a general beneficial effect in different exptl. paradigms disturbing memory performance in rodents. The β-amyloid fragment present in patients with Alzheimer's disease (Aβ1-42, 2 nmol, icv) decreased spontaneous alternation in the Y-maze after 15 days (29%) to an extent similar to the decrease of memory performance caused by scopolamine (2 mg/kg, i.p.) or MK-801 (0.25 mg/kg, i.p.) after 30 min (28% and 39%, resp.). The selective A2A receptor antagonist SCH58261 (0.05 mg/kg, i.p. every 24 h, starting 30 min before the noxious stimuli) prevented Aβ1-42-induced amnesia, but failed to modify scopolamine- or MK-801-induced amnesia. Similar conclusions were reached when testing another A2A receptor antagonist (KW6002, 3 mg/kg, i.p.). These results indicate that A2A receptors do not affect general processes of memory impairment but instead play a crucial role restricted to neurodegenerative conditions involving an insidious synaptic deterioration leading to memory dysfunction.
TI Adenosine A2A receptor blockade prevents memory dysfunction caused by β-amyloid peptides but not by scopolamine or MK-801
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Adenosine A2A receptor blockade prevents memory dysfunction caused by β-amyloid peptides but not by scopolamine or MK-801
AB Adenosine A2A receptor antagonists alleviate memory deficits caused by aging or by administration of β-amyloid peptides in rodents, which is in accordance with the beneficial effects of caffeine consumption (an adenosine receptor antagonist) on memory performance in aged individuals and in preventing Alzheimer's disease. We now tested if A2A receptor blockade affords a general beneficial effect in different exptl. paradigms disturbing memory performance in rodents. The β-amyloid fragment present in patients with Alzheimer's disease (Aβ1-42, 2 nmol, icv) decreased spontaneous alternation in the Y-maze after 15 days (29%) to an extent similar to the decrease of memory performance caused by scopolamine (2 mg/kg, i.p.) or MK-801 (0.25 mg/kg, i.p.) after 30 min (28% and 39%, resp.). The selective A2A receptor antagonist SCH58261 (0.05 mg/kg, i.p. every 24 h, starting 30 min before the noxious stimuli) prevented Aβ1-42-induced amnesia, but failed to modify scopolamine- or MK-801-induced amnesia. Similar conclusions were reached when testing another A2A receptor

antagonist (KW6002, 3 mg/kg, i.p.). These results indicate that A2A receptors do not affect general processes of memory impairment but instead play a crucial role restricted to neurodegenerative conditions involving an insidious synaptic deterioration leading to memory dysfunction.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:588263 CAPLUS Full-text
DOCUMENT NUMBER: 147:378757
TITLE: The effect of striatal dopamine depletion and the adenosine A2A antagonist KW-6002 on reversal learning in rats
AUTHOR(S): O'Neill, Martin; Brown, Verity J.
CORPORATE SOURCE: School of Psychology, University of St. Andrews, Scotland, KY16 9JU, UK
SOURCE: Neurobiology of Learning and Memory (2007), 88(1), 75-81
CODEN: NLMEFR; ISSN: 1074-7427
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study assessed whether dopamine in the dorsomedial striatum is necessary for flexible adaptation to changes in stimulus-response contingencies. As KW-6002 (Istradefylline), an adenosine A2A antagonist, improves motor deficits resulting from striatal dopamine depletion, we also tested for potential ameliorative effects of KW-6002 on dopamine depletion-induced cognitive deficits. Male Lister hooded rats were presented with two bowls, discriminable by either a textured covering on the outer surface, their scent or the bowl contents (digging media) in which bait was buried. Once they had learned in which bowl food was buried, the stimulus-response contingencies were reversed. In both phases (acquisition and reversal), the criterion for learning was defined a priori as six consecutive correct trials. Following depletion of dopamine in the dorsomedial striatum, acquisition of the discriminations was intact but there was an increase in the number of trials to attain criterion performance in the reversal phases, indicating an impairment in reversal learning. KW-6002 (1 mg/kg bidaily for 10 days) non-specifically increased the number of trials to criterion at all stages of the test and in both controls (sham-operated) and dopamine-depleted rats. Chronic KW-6002 treatment did not improve the reversal deficits in dopamine-depleted rats. These findings suggest that dopamine transmission in the dorsomedial striatum is critical for the flexible shifting of response patterns and the ameliorative effects of KW-6002 following depletion of dopamine in the striatum may be restricted to motor functions without relieving deficits in response-shifting flexibility.

TI The effect of striatal dopamine depletion and the adenosine A2A antagonist KW-6002 on reversal learning in rats

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI The effect of striatal dopamine depletion and the adenosine A2A antagonist
KW-6002 on reversal learning in rats

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:547543 CAPLUS Full-text
DOCUMENT NUMBER: 143:53542
TITLE: Xanthine derivatives and salts and compositions for
preventing and/or treating higher brain dysfunction
INVENTOR(S): Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo;
Kobayashi, Minoru; Toki, Shinichiro; Seno, Naoki;
Ikeda, Ken
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056016	A1	20050623	WO 2004-JP18765	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296137	A1	20050623	AU 2004-296137	20041209
CA 2550130	A1	20050623	CA 2004-2550130	20041209
EP 1709966	A1	20061011	EP 2004-807124	20041209

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

CN 1889959	A	20070103	CN 2004-80036267	20041209
BR 2004017241	A	20070306	BR 2004-17241	20041209
US 20070078148	A1	20070405	US 2006-579829	20060517
MX 2006005965	A	20060809	MX 2006-5965	20060525
KR 2006124615	A	20061205	KR 2006-711123	20060607
IN 2006CN02490	A	20070608	IN 2006-CN2490	20060706
PRIORITY APPLN. INFO.:			JP 2003-410432 A	20031209
			WO 2004-JP18765 W	20041209

OTHER SOURCE(S): MARPAT 143:53542

AB A preventive and/or therapeutic agent for higher brain dysfunctions which contains as an active ingredient a xanthine derivative represented, for example, by the following formula (I) or a pharmacol. acceptable salt thereof: (I) (II) wherein R1, R2, and R3 are the same or different and each represents hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; R4 represents cycloalkyl, -(CH2)n-R5, or the formula (II) given above; and X1 and X2 are the same or different and each represents oxygen or sulfur. The higher brain dysfunction includes aging brain damage, brain trauma, cerebrovascular disease, memory disorder, thinking disorder, recognition disorder, behavior disorder, learning disorder, etc.

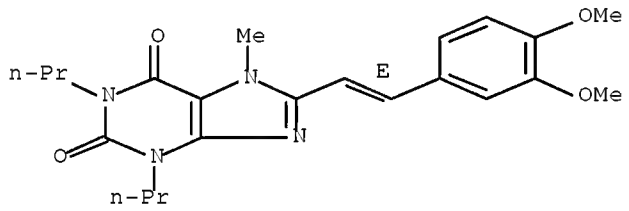
TI Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction

http://www.cas.org/support/stngen/stndoc/properties.html

```
=> e 141807-96-7/rn
E37          1     141807-94-5/RN
E38          1     141807-95-6/RN
E39          1 --> 141807-96-7/RN
E40          1     141807-97-8/RN
E41          1     141807-98-9/RN
E42          1     141807-99-0/RN
E43          1     141808-00-6/RN
E44          1     141808-01-7/RN
E45          1     141808-02-8/RN
E46          1     141808-03-9/RN
E47          1     141808-04-0/RN
E48          1     141808-05-1/RN

=> s e39
L7           1 141807-96-7/RN

=> d l7
```

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 141807-96-7 REGISTRY
ED Entered STN: 12 Jun 1992
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-
    methyl-1,3-dipropyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-
    methyl-1,3-dipropyl-, (E)-
OTHER NAMES:
CN KF 17837
CN KW 17837
FS STEREOSEARCH
MF C22 H28 N4 O4
SR CA
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS,
      EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS*, TOXCENTER, USPAT2,
      USPATFULL
        (*File contains numerically searchable property data)

Double bond geometry as shown.

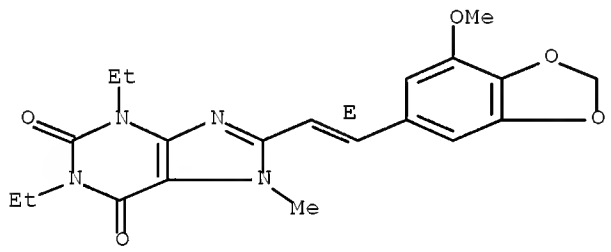


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

55 REFERENCES IN FILE CA (1907 TO DATE)
55 REFERENCES IN FILE CAPLUS (1907 TO DATE)

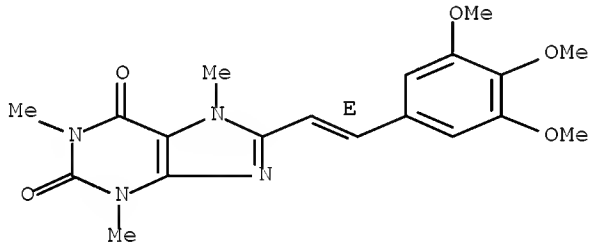
=> e 155272-00-7/rn
E49 1 155271-98-0/RN
E50 1 155271-99-1/RN
E51 1 --> 155272-00-7/RN
E52 1 155272-01-8/RN
E53 1 155272-02-9/RN
E54 1 155272-03-0/RN
E55 1 155272-04-1/RN
E56 1 155272-05-2/RN
E57 1 155272-06-3/RN
E58 1 155272-07-4/RN
E59 1 155272-08-5/RN
E60 1 155272-09-6/RN

```
=> s e51
L8            1 155272-00-7/RN

=> d l8

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155272-00-7  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[(1E)-2-(7-methoxy-
1,3-
     benzodioxol-5-yl)ethenyl]-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-
     benzodioxol-5-yl)ethenyl]-7-methyl-, (E)-
OTHER NAMES:
CN   (E)-1,3-Diethyl-8-(3,4-methylenedioxy-5-methoxystyryl)-7-
methylxanthine
FS   STEREOSEARCH
MF   C20 H22 N4 O5
SR   CA
LC   STN Files:   CA, CAPLUS, RTECS*, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```



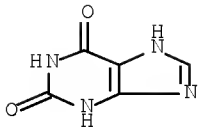

```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              8 REFERENCES IN FILE CA (1907 TO DATE)
              8 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> e 51389-37-8/rn
E61           1     51389-35-6/RN
E62           1     51389-36-7/RN
E63           1 --> 51389-37-8/RN
E64           1     51389-38-9/RN
E65           1     51389-39-0/RN
E66           1     51389-40-3/RN
E67           1     51389-41-4/RN
E68           1     51389-42-5/RN
E69           1     51389-43-6/RN
E70           1     51389-44-7/RN
E71           1     51389-45-8/RN
```

```
E72          1     51389-46-9/RN

=>

=> s e63
L9           1 51389-37-8/RN

=> d l9

L9   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   51389-37-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-
     trimethoxyphenyl)ethenyl]-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-
     trimethoxyphenyl)ethenyl]-, (E)-
OTHER NAMES:
CN   KF 18446
CN   trans-8-(3,4,5-Trimethoxystyryl)caffeine
FS   STEREOSEARCH
MF   C19 H22 N4 O5
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, RTECS*, TOXCENTER,
USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              14 REFERENCES IN FILE CA (1907 TO DATE)
              14 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> e 69-89-6/rn
E73          1     69-81-8/RN
E74          1     69-86-3/RN
E75          1 --> 69-89-6/RN
E76          1     69-90-9/RN
E77          1     69-91-0/RN
E78          1     69-93-2/RN
```

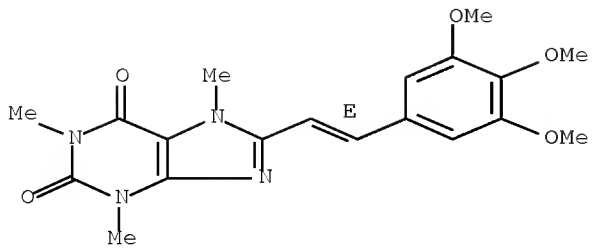
```
E79          1     69-96-5/RN
E80          1     690-00-6/RN
E81          1     690-01-7/RN
E82          1     690-02-8/RN
E83          1     690-03-9/RN
E84          1     690-04-0/RN

=> s e75
L10          1 69-89-6/RN

=> d l10

L10  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   69-89-6  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   1H-Purine-2,6-dione, 3,9-dihydro-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 3,7-dihydro- (9CI)
CN   Xanthine (8CI)
OTHER NAMES:
CN   1H,3H,7H-Xanthine
CN   1H,3H,9H-Xanthine
CN   1H-Purine-2,6-diol
CN   2,6-Dioxo-1,2,3,6-tetrahydropurine
CN   2,6-Dioxopurine
CN   3,9-Dihydro-1H-purine-2,6-dione
CN   3,9-Dihydropurine-2,6-dione
CN   9H-Purine-2,6(1H,3H)-dione
CN   Isoxanthine
CN   NSC 14664
CN   Pseudoxanthine
CN   Purine-2,6(1H,3H)-dione
CN   Xan
CN   Xanthic oxide
CN   Xanthin
DR   16819-86-6, 51953-26-5, 6050-36-8, 6053-41-4, 28522-58-9, 33669-
67-9,
     42911-15-9
MF   C5 H4 N4 O2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
BIOTECHNO,
       CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX,
CHEMLIST, CIN,
       CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT,
IFIUDB,
       IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, RTECS*,
SPECINFO,
       TOXCENTER, USPAT2, USPATFULL, USPATOLD
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5562 REFERENCES IN FILE CA (1907 TO DATE)
926 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5581 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e kf 18446/cn
E85           1     KF 18259/CN
E86           1     KF 18280/CN
E87           1 --> KF 18446/CN
E88           1     KF 18627/CN
E89           1     KF 1935/CN
E90           1     KF 19418/CN
E91           1     KF 19514/CN
E92           1     KF 19631/CN
E93           1     KF 1M/CN
E94           1     KF 1X4/CN
E95           2     KF 2/CN
E96           1     KF 2 (FLUX)/CN

=> s e87
L11           1 "KF 18446"/CN

=> d l11

L11  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   51389-37-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-
     trimethoxyphenyl)ethenyl]-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-
     trimethoxyphenyl)ethenyl]-, (E)-
OTHER NAMES:
CN   KF 18446
CN   trans-8-(3,4,5-Trimethoxystyryl)caffeine
FS   STEREOSEARCH
MF   C19 H22 N4 O5
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, RTECS*, TOXCENTER,
USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```



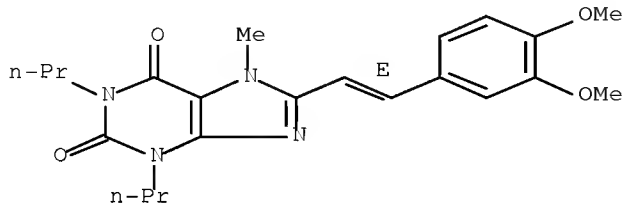
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e kf 17837/cn
E97          1     KF 17625/CN
E98          1     KF 17643/CN
E99          1 --> KF 17837/CN
E100         1     KF 17837S/CN
E101         1     KF 18259/CN
E102         1     KF 18280/CN
E103         1     KF 18446/CN
E104         1     KF 18627/CN
E105         1     KF 1935/CN
E106         1     KF 19418/CN
E107         1     KF 19514/CN
E108         1     KF 19631/CN

=> s e99
L12          1 "KF 17837"/CN

=> d l12

L12  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   141807-96-7  REGISTRY
ED   Entered STN:  12 Jun 1992
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-
dihydro-7-
     methyl-1,3-dipropyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-
dihydro-7-
     methyl-1,3-dipropyl-, (E)-
OTHER NAMES:
CN   KF 17837
CN   KW 17837
FS   STEREOSEARCH
MF   C22 H28 N4 O4
SR   CA
LC   STN Files:   ADISINSIGHT, BEILSTEIN*, BIOSIS, BIOTECHNO, CA,
CAPLUS,
```

EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS*, TOXCENTER, USPAT2,
USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



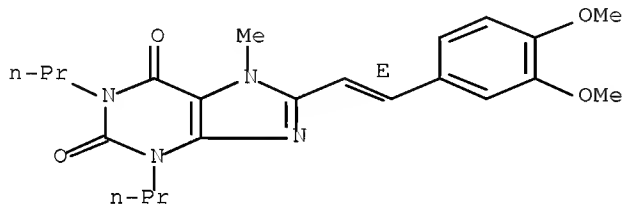
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

55 REFERENCES IN FILE CA (1907 TO DATE)
55 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e kw 17837/cn
E109          1     KW 139/CN
E110          1     KW 1539/CN
E111          1 --> KW 17837/CN
E112          1     KW 1937/CN
E113          1     KW 1938/CN
E114          1     KW 1976/CN
E115          1     KW 2/CN
E116          1     KW 2000/CN
E117          1     KW 2007/CN
E118          1     KW 2030/CN
E119          1     KW 2083/CN
E120          1     KW 2100/CN

=> s e111
L13           1 "KW 17837"/CN

=> d l13

L13  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   141807-96-7  REGISTRY
ED   Entered STN:  12 Jun 1992
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-
dihydro-7-
     methyl-1,3-dipropyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-
dihydro-7-
     methyl-1,3-dipropyl-, (E)-
OTHER NAMES:
CN   KF 17837
CN   KW 17837
```

FS STEREOSEARCH
MF C22 H28 N4 O4
SR CA
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS,
      EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, RTECS*, TOXCENTER, USPAT2,
      USPATFULL
        (*File contains numerically searchable property data)

Double bond geometry as shown.



This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s (l7 or l9 or l11 or l12 or l13)
            55 L7
            14 L9
            14 L11
            55 L12
            55 L13
L14         58 (L7 OR L9 OR L11 OR L12 OR L13)

=> s l14 and brain, disease/it
        495101 BRAIN/IT
          2040 BRAINS/IT
        495220 BRAIN/IT
                 ((BRAIN OR BRAINS)/IT)
        867672 DISEASE/IT
        105349 DISEASES/IT
        913630 DISEASE/IT
                 ((DISEASE OR DISEASES)/IT)
         71978 BRAIN, DISEASE/IT
                 ((BRAIN(W)DISEASE)/IT)
L15          1 L14 AND BRAIN, DISEASE/IT

=> s l14 and learning disorders/it
         18467 LEARNING/IT
             4 LEARNINGS/IT
         18470 LEARNING/IT
                 ((LEARNING OR LEARNINGS)/IT)
        145760 DISORDERS/IT
          1263 LEARNING DISORDERS/IT
                 ((LEARNING(W)DISORDERS)/IT)
L16          1 L14 AND LEARNING DISORDERS/IT

=> s l14 and mental and behavioral disorders/it
```

```
         66412 MENTAL
             5 MENTALS
         66416 MENTAL
                 (MENTAL OR MENTALS)
         31717 BEHAVIORAL/IT
         31717 BEHAVIORAL/IT
                 ((BEHAVIORAL OR BEHAVIOURAL)/IT)
        145760 DISORDERS/IT
         20949 BEHAVIORAL DISORDERS/IT
                 ((BEHAVIORAL(W)DISORDERS)/IT)
L17          2 L14 AND MENTAL AND BEHAVIORAL DISORDERS/IT

=> s l14 and memory, biological/it
        104513 MEMORY/IT
          1779 MEMORIES/IT
        104686 MEMORY/IT
                 ((MEMORY OR MEMORIES)/IT)
       3903901 BIOLOGICAL/IT
           537 BIOLOGICALS/IT
       3904271 BIOLOGICAL/IT
                 ((BIOLOGICAL OR BIOLOGICALS)/IT)
        246352 BIOL/IT
            12 BIOLS/IT
        246362 BIOL/IT
                 ((BIOL OR BIOLS)/IT)
       4062690 BIOLOGICAL/IT
                 ((BIOLOGICAL OR BIOL)/IT)
         18207 MEMORY, BIOLOGICAL/IT
                 ((MEMORY(W)BIOLOGICAL)/IT)
L18          1 L14 AND MEMORY, BIOLOGICAL/IT

=> s l14 and (learning or amnesia or dopamin? or motor? or ?acognit?)
         42736 LEARNING
           105 LEARNINGS
         42830 LEARNING
                 (LEARNING OR LEARNINGS)
          3941 AMNESIA
            23 AMNESIAS
          3945 AMNESIA
                 (AMNESIA OR AMNESIAS)
        108298 DOPAMIN?
        152363 MOTOR?
        367914 ENGINE?
        507815 MOTOR?
                 (MOTOR? OR ENGINE?)
            70 ?ACOGNIT?
L19         10 L14 AND (LEARNING OR AMNESIA OR DOPAMIN? OR MOTOR? OR
?ACOGNIT?)

=> s l19 and (py<2003 or ay<2003 or pry<2003)
      22983605 PY<2003
       4504987 AY<2003
       3974028 PRY<2003
L20          6 L19 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d l20 ibib abs ti hit 1-20
```

L20 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:570030 CAPLUS Full-text
DOCUMENT NUMBER: 141:99661
TITLE: Identification of compounds suitable as agonists and/or antagonists of adenosine A2A receptor coupled to specific G proteins, and use of identified compounds in treatment of various disorders in mammals
INVENTOR(S): Fredholm, Bertil B.; Kull, Bjoern
PATENT ASSIGNEE(S): Actar Ab, Swed.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058974	A1	20040715	WO 2003-SE2086	20031229 <--
AU 2003291608	A1	20040722	AU 2003-291608	20031229 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-436480P P 20021227 <--
WO 2003-SE2086 W 20031229

AB The invention discloses a method of drug screening to select chemical compds. suitable as receptor agonists or antagonists that act on a receptor belonging to the family of G protein coupled receptors. The method involves constructing a biol. preparation comprising a receptor coupled to a specific G protein, bringing a compound in contact with said preparation, and studying the functional properties of said compound in biol. preparation The invention also discloses the use of identified compound as a drug

for treatment of CNS disorders, cardiovascular disorders, inflammatory disorders, metabolic disorders, cancer and other hyperproliferative disorders in a mammal. Specifically, the invention discloses a novel approach to identify and test compds. based on changes in adenosine A2A receptor binding dependent on the nature of the coupled G protein. The invention related that this approach seemed feasible due to the evidence that G proteins, such as Gs, Gi or Golf, influence the binding properties of A2A receptors. The invention also related that a truly efficient drug mol., in addition to affinity towards A2A, can be specific towards the different G proteins associated with A2A. In the examples, the invention used transformed CHO cells expressing A2A receptors linked to Gs or Golf G proteins, and demonstrated the existence of G-protein-dependent ligand specificity. Specifically, the examples demonstrated that substance KF 17837 has higher affinity to the A2A-Golf complex in striatum than to A2A-Gs complex in leukocytes. The examples also showed how some compds. influence A2A receptors coupled to Golf more readily than A2A receptors coupled to Gs.

TI Identification of compounds suitable as agonists and/or antagonists of
adenosine A2A receptor coupled to specific G proteins, and use of identified compounds in treatment of various disorders in mammals

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PRAI US 2002-436480P P 20021227 <--
WO 2003-SE2086 W 20031229

IT Central nervous system, disease
(dopamine-related; method of drug screening to select agonists or antagonists of G protein coupled receptors, and use of
identified drug in treatment of various disorders including)

IT 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method of drug screening to select agonists or antagonists of G
protein coupled receptors, and use of identified drug in treatment of
various disorders including dopamine-related CNS disorders)

IT 141607-96-7, KF 17837
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substance KF 17837 has higher affinity to A2A receptor -Golf complex
in striatum than to A2A-Gs complex in leukocytes)

L20 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:793451 CAPLUS Full-text
DOCUMENT NUMBER: 137:289033
TITLE: Adenosine A2A receptor antagonists combined with
neurotrophic activity compounds in the treatment of
Parkinson's disease
INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen,

Karin
Sandager
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080957	A1	20021017	WO 2002-DK228	20020404 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440196	A1	20021017	CA 2002-2440196	20020404 <--
AU 2002338309	A1	20021021	AU 2002-338309	20020404 <--
EP 1379269	A1	20040114	EP 2002-759761	20020404 <--
EP 1379269	B1	20090304		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004529916	T	20040930	JP 2002-578996	20020404 <--
US 20040097540	A1	20040520	US 2003-473809	20031002 <--
US 7160899	B2	20070109		
MX 2003009185	A	20040217	MX 2003-9185	20031008 <--
PRIORITY APPLN. INFO.:			DK 2001-583 A	20010409 <--
			WO 2002-DK228 W	20020404 <--

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of

KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H- pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3- dione-3-oxime; GDNF; Neublastin; and pharmaceutically acceptable salts thereof.

TI Adenosine A2A receptor antagonists combined with neurotrophic activity
compounds in the treatment of Parkinson's disease

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI WO 2002080957 A1 20021017

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002080957	A1	20021017	WO 2002-DK228	20020404 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2440196	A1	20021017	CA 2002-2440196	20020404 <--
	AU 2002338309	A1	20021021	AU 2002-338309	20020404 <--
	EP 1379269	A1	20040114	EP 2002-759761	20020404 <--
	EP 1379269	B1	20090304		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004529916	T	20040930	JP 2002-578996	20020404 <--
	US 20040097540	A1	20040520	US 2003-473809	20031002 <--
	US 7160899	B2	20070109		
	MX 2003009185	A	20040217	MX 2003-9185	20031008 <--
PRAI	DK 2001-583	A	20010409 <--		
	WO 2002-DK228	W	20020404 <--		

IT Nerve

(dopaminergic; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT Brain
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine A2A receptor antagonists combined with neurotrophic compds.
in treatment of Parkinson's disease)

IT 14114-46-6, DMPX 104615-18-1, CGS-15943 139180-30-6, ZM-241385 141807-96-7, KF-17837 155270-99-8, KW-6002 160098-96-4, SCH-58261 160753-58-2 309711-72-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonists combined with neurotrophic compds.
in treatment of Parkinson's disease)

L20 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:943 CAPLUS Full-text
DOCUMENT NUMBER: 137:88308
TITLE: Adenosine A2A receptor antagonists: Potential therapeutic and neuroprotective effects in Parkinson's disease
AUTHOR(S): Morelli, M.; Wardas, J.
CORPORATE SOURCE: Department of Toxicology, University of Cagliari, Palazzo delle Scienze, Cagliari, 09124, Italy
SOURCE: Neurotoxicity Research (2001), 3(6), 545-556
CODEN: NURRFI; ISSN: 1029-8428
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The most effective treatment of Parkinson's disease (PD) is, at present, the dopamine precursor L-3,4-dihydroxyphenyl-alanine (L-DOPA), however a number of disadvantages such as a loss of drug efficacy and severe side-effects (psychoses, dyskinesias and on-off phenomena) limit long-term, effective utilization of this drug. Recent exptl. studies in which selective antagonists of adenosine A2A receptors were used, have shown an improvement in motor disabilities in animal models of PD. The A2A antagonist [7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo- (4,3-e)-1,2,4-triazolo(1,5--c)pyrimidine] (SCH 58261) potentiated the contralateral turning behavior induced by a threshold dose of L-DOPA or direct dopamine receptor agonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, an effect accompanied by an increase in Foslike-immunoreactivity in neurons of the lesioned striatum. Likewise, other A2A receptor antagonists such as (3,7-dimethyl-1-propargylxanthine) (DMPX), [E-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] (KF 17837) and [E-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2, 6-dione] (KW 6002) antagonized catalepsy induced by haloperidol or reserpine in the rat, whereas in non-human primate models of PD, KW 6002 reduced the rigidity and improved the disability score of

MPTP-treated marmosets and cynomolgus monkeys. Moreover, in contrast to L-DOPA, selective A2A receptor antagonists administered chronically did not produce dyskinesias and did not evoke tolerance in 6-OHDA and MPTP models of PD. An addnl. therapeutic potential of adenosine A2A antagonists emerged from studies showing neuroprotective properties of these compds. in animal models of cerebral ischemia and excitotoxicity, as well as in the (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) (MPTP) model of PD. Adenosine A2A receptor antagonists by reversing motor impairments in animal models of PD and by contrasting cell degeneration are some of the most promising compds. for the treatment of PD.

TI Adenosine A2A receptor antagonists: Potential therapeutic and neuroprotective effects in Parkinson's disease

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Neurotoxicity Research (2001), 3(6), 545-556
CODEN: NURRFI; ISSN: 1029-8428

L20 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:828333 CAPLUS Full-text
DOCUMENT NUMBER: 134:157476

TITLE: Adenosine A2A receptor antagonists KF17837 and KW-6002 potentiate rotation induced by dopaminergic drugs in hemi-Parkinsonian rats

AUTHOR(S): Koga, K.; Kurokawa, M.; Ochi, M.; Nakamura, J.; Kuwana, Y.
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co. Ltd., Shizuoka, Sunto-gun, Nagaizumi-cho, 411-8731, Japan

SOURCE: European Journal of Pharmacology (2000), 408(3), 249-255
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of novel adenosine A2A receptor antagonists KF17837 ((E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine- 2,6-dione) and KW-6002 ((E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl- 3,7-dihydro-1H-purine-2,6-dione), on rotational behavior induced by apomorphine or L-DOPA (l-3,4-dihydroxyphenylalanine) were investigated in rats with unilateral 6-hydroxydopamine lesions. Both KF17837 and KW-6002 slightly induced rotational behavior per se. However, KF17837 and KW-6002 significantly increased the total counts of turning induced by apomorphine at doses of 3 mg/kg, p.o. and 10 mg/kg, p.o., and at doses of 1 mg/kg, p.o. and higher, resp. KF17837 and KW-6002 also potentiated the rotational behavior induced by L-DOPA at a dose of 3 mg/kg, p.o. Furthermore, i.c.v. injection (10 μg/20 μl) of a selective adenosine A2 receptor agonist CGS 21680 {2-[p-(2-carboxyethyl)phenethylamino]-5'-N- ethylcarboxamidoadenosine}

partially prevented the rotational behavior induced by apomorphine and this inhibition was reversed by KW-6002 (1 mg/kg, p.o.). The increase in total counts of apomorphine-induced turning by the adenosine A2A receptor antagonists seems to be mainly attributable to prolongation of turning duration rather than enhancement of intensity. These results suggest that these adenosine A2A receptor antagonists may be useful to ameliorate shortening in the duration of dopaminergic drug response in patients with advanced Parkinson's disease.

TI Adenosine A2A receptor antagonists KF17837 and KW-6002 potentiate rotation
induced by dopaminergic drugs in hemi-Parkinsonian rats

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Adenosine A2A receptor antagonists KF17837 and KW-6002 potentiate rotation
induced by dopaminergic drugs in hemi-Parkinsonian rats

L20 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:394679 CAPLUS Full-text
DOCUMENT NUMBER: 129:118143
ORIGINAL REFERENCE NO.: 129:24113a,24116a
TITLE: Pharmacological characterization of a simple behavioral response mediated selectively by central adenosine A1 receptors, using in vivo and in vitro techniques
AUTHOR(S): Marston, Hugh M.; Finlayson, Keith; Maemoto, Takuya; Olverman, Henry J.; Akahane, Atsushi; Sharkey, John; Butcher, Steven P.
CORPORATE SOURCE: Fujisawa Institute of Neuroscience, University of Edinburgh, Edinburgh, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 285(3), 1023-1030
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The behavioral profile of a range of adenosine receptor ligands was examined in rats using a locomotor activity model. Adenosine receptor agonists, including the selective A1 receptor agonist, N6-cyclopentyladenosine (CPA) and the A2A agonist, 2-[(2-aminoethylamino)carbonylethyl-phenylethylamino]- 5'-ethylcarboxamidoadenosine (APEC), reduced spontaneous motor activity in a dose-dependent manner. CPA-induced locomotor depression was attenuated by adenosine A1 receptor selective antagonists, such as 8-cyclopentyl-1,3-dipropylxanthine (DPCPX), (R)-1-[(E)-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-2-piperidine ethanol (FK453), and (R)-1-[(E)-3-(2-

phenylpyrazolo[1,5-a]pyridin-3-yl)- acryloyl]-piperidin-2-yl acetic acid (FK352), but not by the A2A receptor antagonist, (E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthine (KF17837). By contrast, APEC-induced hypolocomotion was attenuated by KF17837 but not by DPCPX, confirming that adenosine A1 and A2A receptor activation mediates locomotor output independently. Two peripheral adenosine receptor antagonists, 8-(p-sulfophenyl)-1,3-dipropylxanthine (DPSPX) and 8-(p-sulfophenyl)-1,3-dimethylxanthine (8-PST), did not alter CPA-induced hypolocomotion. This confirmed that pharmacol. reversal of the adenosine A1 receptor-mediated response involved a central site of drug action. The relationship between occupancy of central adenosine A1 receptors and behavioral effect was therefore assessed. Regression anal. on log transformed data confirmed assocns. between antagonist affinity for brain [3H]DPCPX binding sites and, in order of increasing significance, the equivalent behavioral dose (EBD) for reversal of CPA-induced hypolocomotion (R2 = 0.32), the serum concentration of drug (R2 = 0.65), and most significantly with the brain concentration of drug detected 20 min after administration of the (EBD) (R2 = 0.95). These data suggest that competition between agonists and antagonists, for occupancy of central adenosine A1 receptors, is intrinsic to the pharmacol. reversal of CPA- induced hypolocomotion. The validity of the model as a simple predictive screen for the blood/brain barrier permeability of adenosine A1 receptor antagonists was thereby confirmed.

L20 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

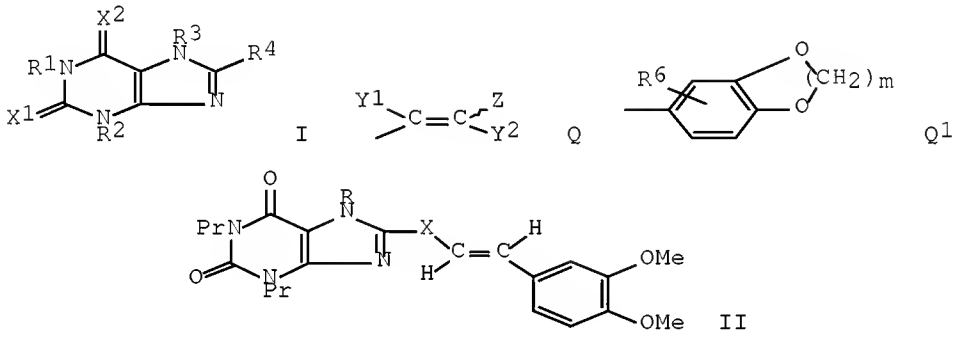
ACCESSION NUMBER: 1994:315658 CAPLUS Full-text
DOCUMENT NUMBER: 120:315658
ORIGINAL REFERENCE NO.: 120:55249a,55252a
TITLE: KF17837: a novel selective adenosine A2A receptor antagonist with anticataleptic activity
AUTHOR(S): Kanda, Tomoyuki; Shiozaki, Shizuo; Shimada, Junichi; Suzuki, Fumio; Nakamura, Joji
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., 1188 Shimotogari, Nagaizumi-Cho, Sunto-Gun, Shizuoka, 411, Japan
SOURCE: European Journal of Pharmacology (1994), 256(3), 263-8
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KF17837 is a novel selective adenosine A2A receptor antagonist. Oral administration of KF17837 (2.5, 10.0 and 30.0 mg/kg) significantly ameliorated the cataleptic responses induced by intracerebroventricular administration of an adenosine A2A receptor agonist, CGS 21680 (10 μg), in a dose-dependent manner. KF17837 also reduced the catalepsy induced by haloperidol (1 mg/kg i.p.) and by reserpine (5 mg/kg i.p.). These anticataleptic effects were exhibited dose dependently at doses from 0.625 and 2.5 mg/kg p.o., resp. Moreover, KF17837 (0.625 mg/kg p.o.) potentiated the anticataleptic effects of a subthreshold dose of L-3,4-dihydroxyphenylalanine (L-DOPA; 25 mg/kg i.p.) plus

benserazide (6.25 mg/kg i.p.). These results suggested that KF17837 is a centrally active adenosine A2A receptor antagonist and that the dopaminergic function of the nigrostriatal pathway is potentiated by adenosine A2A receptor antagonists. Furthermore, KF17837 may be a useful drug in the treatment of parkinsonism.
TI KF17837: a novel selective adenosine A2A receptor antagonist with anticataleptic activity

```
=> s l14 and (py<2003 or ay<2003 or pry<2003)
      22983605 PY<2003
       4504987 AY<2003
       3974028 PRY<2003
L21          43 L14 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d l21 ibib abs ti hit 33-43

L21  ANSWER 33 OF 43  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        1994:483358  CAPLUS  Full-text
DOCUMENT NUMBER:         121:83358
ORIGINAL REFERENCE NO.:  121:14985a,14988a
TITLE:                   preparation of xanthine derivatives as
antidepressants
INVENTOR(S):             Suzuki, Fumio; Shimada, Junichi; Ishii, Akio;
                         Nakamura, Joji; Ichikawa, Shunji; Kitamura,
Shigeto;
                         Koike, Nobuaki
PATENT ASSIGNEE(S):      Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE:                  PCT Int. Appl., 173 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                Japanese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------------    ----   --------    --------------------   ----
----
     WO 9401114           A1    19940120    WO 1993-JP931
19930707 <--
         W:  CA, JP, NO, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE
     EP 628311            A1    19941214    EP 1993-914963
19930707 <--
     EP 628311            B1    20020424
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,
NL, PT, SE
     JP 2928386           B2    19990803    JP 1993-502746
19930707 <--
     AT 216584            T     20020515    AT 1993-914963
19930707 <--
     PT 628311            T     20020930    PT 1993-914963
19930707 <--
     ES 2176204           T3    20021201    ES 1993-914963
19930707 <--
     CA 2116967           C     20030819    CA 1993-2116967
```

19930707 <--
US 5543415 A 19960806 US 1994-199142
19940225 <--
NO 9400737 A 19940503 NO 1994-737
19940303 <--
PRIORITY APPLN. INFO.: JP 1992-181025 A
19920708 <--
WO 1993-JP931 W
19930707 <--
OTHER SOURCE(S): MARPAT 121:83358
GI



AB Xanthine derivs. [I; R1, R2, R3 = H, alkyl, allyl, propargyl; R4 = cycloalkyl, -(CH2)nR5 (wherein R5 = optionally substituted aryl, heterocyclic group, and n = 0-4), Q (wherein Y1, Y2 = H, F, Me; Z = optionally substituted aryl, Q1 wherein R6 = H, OH, alkyl, alkoxy, halo, nitro or amino; m = 1-3), optionally substituted heterocyclic group; X1, X2 = O or S] are prepared A mixture of 5,6-diamino-1,3-dipropyluracil, 3,4-dimethoxycinnamic acid, and 3-(3-diethylaminopropyl)-1- ethylcarbodiimide HCl in dioxane-H2O was stirred at room temperature and pH 5.5 to give 94% amide II (R = H, X = NHCO), which was refluxed with 1N NaOH in dioxane to give 77% styryl compound II (R = H, X = bond) (III). Methylation of III with MeI and K2CO3 in DMF at 50° gave 98% Me derivative II (R = Me, X = bond), which at 2.5 mg/kg p.o. in mice showed 4.8-fold increase in clonidine-induced aggression, vs. control.
TI preparation of xanthine derivatives as antidepressants
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT
PI WO 9401114 A1 19940120

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9401114	A1	19940120	WO 1993-JP931	19930707 <--

W: CA, JP, NO, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 628311 A1 19941214 EP 1993-914963
19930707 <--
EP 628311 B1 20020424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,
NL, PT, SE
JP 2928386 B2 19990803 JP 1993-502746
19930707 <--
AT 216584 T 20020515 AT 1993-914963
19930707 <--
PT 628311 T 20020930 PT 1993-914963
19930707 <--
ES 2176204 T3 20021201 ES 1993-914963
19930707 <--
CA 2116967 C 20030819 CA 1993-2116967
19930707 <--
US 5543415 A 19960806 US 1994-199142
19940225 <--
NO 9400737 A 19940503 NO 1994-737
19940303 <--
PRAI JP 1992-181025 A 19920708 <--
WO 1993-JP931 W 19930707 <--

L21 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:473411 CAPLUS Full-text
DOCUMENT NUMBER: 121:73411
ORIGINAL REFERENCE NO.: 121:12911a,12914a
TITLE: Effects of the new A2 adenosine receptor antagonist
8FB-PTP, an 8 substituted pyrazolo-triazolo-pyrimidine, on in vitro functional
models
AUTHOR(S): Dionisotti, Silvio; Conti, Annamaria; Sandoli, Daniele; Zocchi, Cristina; Gatta, Franco; Ongini,
Ennio
CORPORATE SOURCE: Res. Lab., Schering-Plough S.p.A., Comazzo, 20060,
Italy
SOURCE: British Journal of Pharmacology (1994), 112(2), 659-65
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have characterized the in vitro pharmacol. profile of putative A2 adenosine antagonists, two non-xanthine compds., 5-amino-8-(4-fluorobenzyl)-2-(2-furyl)-pyrazolo [4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine (8FB-PTP) and 5-amino-9-chloro-2-(2-furyl)- 1,2,4-triazolo[1,5-c]quinazoline (CGS 15943), and the xanthine derivative (E)7-methyl-8-(3,4-dimethoxystyryl)-1,3-dipropyl-xanthine (KF 17837). In binding studies on bovine brain, 8FB-PTP was the most potent (K1 = 0.074 nM) and selective (28 fold) drug on A2 receptors, whereas CGS 15943 and KF 17837 exhibited affinity in the low and high nanomolar range, resp., and showed little selectivity. In functional studies, 8FB-PTP antagonized 5'-N-ethylcarboxamidoadenosine (NECA)-induced

vasorelaxation of bovine coronary artery (pA2 = 7.98) and NECA-induced inhibition of rabbit platelet aggregation (pA2 = 8.20). CGS 15943 showed weak activity in the platelet aggregation model (pA2 = 7.43) and failed to antagonized NECA-induced vasodilation. KF 17837 was ineffective in both models up to micromolar concns. Antagonism of A1-mediated responses was tested vs. 2-chloro-N6-cyclopentyladenosine (CCPA) in rat atria. 8FB-PTP and CGS 15943 also antagonized competitively the neg. chronotropic response induced by CCPA. Conversely, KF 17837 was unable to reverse A1-mediated responses. 8FB-PTP is a potent and competitive antagonist of responses mediated by A2 adenosine receptors. The data provided a basis to reduce, by further chemical modifications, the affinity at A1 receptor and therefore enhance A2 receptor selectivity.

TI Effects of the new A2 adenosine receptor antagonist 8FB-PTP, an 8 substituted pyrazolo-triazolo-pyrimidine, on in vitro functional models

SO British Journal of Pharmacology (1994), 112(2), 659-65
CODEN: BJPCBM; ISSN: 0007-1188

IT 104615-18-1, CGS 15943 141807-96-7, KF 17837 154910-02-8
RL: BIOL (Biological study)
(pharmacol. profile of, as A2 adenosine receptor antagonist)

L21 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:426752 CAPLUS Full-text
DOCUMENT NUMBER: 121:26752
ORIGINAL REFERENCE NO.: 121:4705a,4708a
TITLE: KF17837 ((E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine), a potent and selective adenosine A2 receptor antagonist
AUTHOR(S): Nonaka, Hiromi; Ichimura, Michio; Takeda, Masami; Nonaka, Yoshiko; Shimada, Jyunichi; Suzuki, Fumio; Yamaguchi, Kazuo; Kase, Hiroshi
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., 1188 Shimotogari, Sunto, Shizuoka, 411, Japan
SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1994), 267(3), 335-41
CODEN: EJPPET; ISSN: 0922-4106
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 8-(3,4-Dimethoxystyryl)-1,3-dipropyl-7-methylxanthine exhibited high affinity and selectivity for adenosine A2A receptors in binding assay using rat striatal A2A receptors labeled with [3H]2-[p-(2-carboxyethyl)-phenethylamino]-5'-N-ethylcarboxamidoadenosine (CGS21680). The affinity was stereo selective: the E isomer, KF17837, showed a Ki value of 1.0±0.057 nM for the A2A receptors, whereas the Z isomer showed much lower affinity. KF17837 had 62-fold selectivity for the A2A receptors vs. rat forebrain A1 receptors labeled with [3H]N6-cyclohexyladenosine (CHA). KF17837 was rapidly photoisomerized to form a stable equilibrium mixture

(18% E - 82% Z), KF17837S, which showed Ki values of 7.9±0.055 nM and 390±68 nM for the A2A and A1 receptors, resp. The inhibition type was competitive for [3H]CGS21680 binding. In rat pheochromocytoma PC12 cells KF17837S antagonized cAMP accumulation induced by 1 μM CGS21680 via the A2A receptors, with an IC50 value of 53±10 nM. cAMP accumulation induced by 10 μM 5'-N-ethylcarboxamidoadenosine via the A2B receptors in Jurkat cells (human T-cell line) was inhibited by KF17837S with an IC50 value of 1500±290 nM. These results indicate that KF17837S (and hence KF17837) is a highly potent and selective adenosine A2A receptor antagonist.

TI KF17837 ((E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine), a potent and selective adenosine A2 receptor antagonist

SO European Journal of Pharmacology, Molecular Pharmacology Section (1994), 267(3), 335-41
CODEN: EJPPET; ISSN: 0922-4106

IT 141807-96-7, KF17837 149744-74-1, KF 17837S
RL: BIOL (Biological study)
(as potent and selective adenosine A2A receptor antagonist)

L21 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:315658 CAPLUS Full-text
DOCUMENT NUMBER: 120:315658
ORIGINAL REFERENCE NO.: 120:55249a,55252a
TITLE: KF17837: a novel selective adenosine A2A receptor antagonist with anticataleptic activity
AUTHOR(S): Kanda, Tomoyuki; Shiozaki, Shizuo; Shimada, Junichi; Suzuki, Fumio; Nakamura, Joji
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., 1188 Shimotogari, Nagaizumi-Cho, Sunto-Gun, Shizuoka, 411, Japan
SOURCE: European Journal of Pharmacology (1994), 256(3), 263-8
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KF17837 is a novel selective adenosine A2A receptor antagonist. Oral administration of KF17837 (2.5, 10.0 and 30.0 mg/kg) significantly ameliorated the cataleptic responses induced by intracerebroventricular administration of an adenosine A2A receptor agonist, CGS 21680 (10 μg), in a dose-dependent manner. KF17837 also reduced the catalepsy induced by haloperidol (1 mg/kg i.p.) and by reserpine (5 mg/kg i.p.). These anticataleptic effects were exhibited dose dependently at doses from 0.625 and 2.5 mg/kg p.o., resp. Moreover, KF17837 (0.625 mg/kg p.o.) potentiated the anticataleptic effects of a subthreshold dose of L-3,4-dihydroxyphenylalanine (L-DOPA; 25 mg/kg i.p.) plus benserazide (6.25 mg/kg i.p.). These results suggested that KF17837 is a centrally active adenosine A2A receptor antagonist and that the dopaminergic function of the nigrostriatal pathway is

potentiated by adenosine A2A receptor antagonists. Furthermore, KF17837 may be a useful drug in the treatment of parkinsonism.

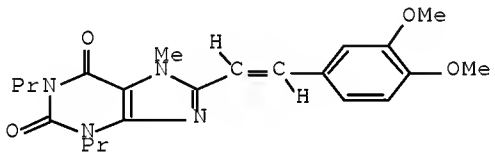
TI KF17837: a novel selective adenosine A2A receptor antagonist with anticataleptic activity

SO European Journal of Pharmacology (1994), 256(3), 263-8
CODEN: EJPHAZ; ISSN: 0014-2999

IT 141807-96-7, KF17837
RL: BIOL (Biological study)
(adenosine A2A receptor antagonist, dopaminergic function potentiation
by, anticataleptic effects in relation to)

L21 ANSWER 37 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:236103 CAPLUS Full-text
DOCUMENT NUMBER: 120:236103
ORIGINAL REFERENCE NO.: 120:41569a,41572a
TITLE: KF17837 is an A2 adenosine receptor antagonist in vivo
AUTHOR(S): Jackson, Edwin K.; Herzer, William A.; Suzuki, Fumio
CORPORATE SOURCE: Med. Cent., Univ. Pittsburgh, Pittsburgh, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics
(1993), 267(3), 1304-10
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The goal of this study was to determine whether KF17837 (I) is a useful pharmacol. probe for investigating in the rat the in vivo physiol. roles of A2 adenosine receptors. In anesthetized rats, bradycardic responses to N6-cyclopentyladenosine and hypotensive responses to 2-[p-(2-carboxyethyl)phenethylamino]-5'-N-ethylcarboxamido adenosine (CGS21680C) were used to assess A1 receptor and A2 receptor activation, resp. After obtaining control responses to N6-cyclopentyladenosine and CGS21680C, the rats received infusions of either vehicle or one of two dosage levels of KF17837, a compound recently demonstrated to be a potent and selective A2 receptor antagonist in vitro. KF17837 was infused for 4 h and, at various times during the infusions, bradycardic and hypotensive responses to N6-cyclopentyladenosine and CGS21680C, resp., were elicited. Infusion of either 10 or 30 μg kg-1 min-1 (2.4 or 7.4 mg kg-1 4 h-1) of KF17837 did not significantly affect the bradycardic responses to N6-

cyclopentyladenosine. By contrast, 10 μg kg-1 min-1 of KF17837 attenuated and 30 μg kg-1 min-1 of KF17837 nearly abolished hypotensive responses to CGS21680C. In a second study, pretreatment with KF17837 (30 μg kg-1 min-1) did not affect the hypotensive response to either PGI2 (3 μg kg-1 min-1) or acetylcholine (100 μg kg-1 min-1); however, it attenuated the hypotensive response to adenosine (300 μg kg-1 min-1). In a third study, hypotension was induced and maintained with an infusion of adenosine (300 μg kg-1 min-1). Subsequent initiation of an infusion of KF17837 (30 μg kg-1 min-1) completely reversed the adenosine-induced hypotension. This study suggests that in vivo KF17837 has relative selectivity for the A2 receptor and may be a useful pharmacol. probe for elucidating the role of endogenous adenosine-A2 receptor interactions in vivo in the rat.

TI KF17837 is an A2 adenosine receptor antagonist in vivo

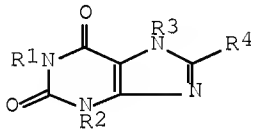
SO Journal of Pharmacology and Experimental Therapeutics (1993), 267(3), 1304-10
CODEN: JPETAB; ISSN: 0022-3565

IT 141807-96-7, KF 17837
RL: BIOL (Biological study)
(A2 adenosine receptor antagonism by, specificity of)

L21 ANSWER 38 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:144161 CAPLUS Full-text
DOCUMENT NUMBER: 120:144161
ORIGINAL REFERENCE NO.: 120:25227a,25230a
TITLE: Pharmaceutical compositions containing xanthine derivatives for treatment of Parkinson's disease
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Ichikawa, Shunji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 565377	A1	19931013	EP 1993-302780	19930408 <--
EP 565377	B1	19980107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2093403	A1	19931009	CA 1993-2093403	19930405 <--
CA 2093403	C	19990810		
NO 9301317	A	19931011	NO 1993-1317	19930406 <--
NO 303265	B1	19980622		
JP 06016559	A	19940125	JP 1993-81953	

19930408 <--
JP 2613352 B2 19970528
AT 161723 T 19980115 AT 1993-302780
19930408 <--
ES 2112386 T3 19980401 ES 1993-302780
19930408 <--
PRIORITY APPLN. INFO.: JP 1992-87115 A
19920408 <--
OTHER SOURCE(S): MARPAT 120:144161
GI



I

AB Pharmaceutical compns. containing xanthine derivs. (I; R1, R2, R3=H, C1-6 alkyl or allyl; R4= C3-8 cycloalkyl) are useful for treatment of Parkinson's disease. (E)-6-amino-5-(3,4-dimethyoxycinnamoyl)amino-1,3- dipropyluracil (preparation is given) was refluxed in NaOH solution, then was neutralized and the deposited crysts. were separated to to obtain (E)-8-(3,4-dimethyoxstyryl)-1,3-dipropylxanthine (II). To II in DMF was added K2CO3 and MeI and the mixture was heated at 50° for 30min followed by filteration and addition of water. The filtrate was extracted with CHCl3 and the extract was washed, dried, evaporated, and purified to obtain (E)-8-(3,4-dimethyoxystyryl)-7-methyl-1,3-dipropylxantha=ine (III). A tablet contained III 20, lactose 143.4, potato starch 30, hydroxypropyl cellulose 6, and Mg stearate 0.6mg.

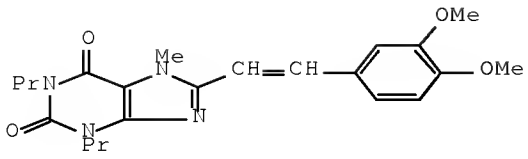
TI Pharmaceutical compositions containing xanthine derivatives for treatment of Parkinson's disease

PI EP 565377 A1 19931013

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 565377	A1	19931013	EP 1993-302780	
19930408 <--				
EP 565377	B1	19980107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2093403	A1	19931009	CA 1993-2093403	
19930405 <--				
CA 2093403	C	19990810		
NO 9301317	A	19931011	NO 1993-1317	
19930406 <--				
NO 303265	B1	19980622		
JP 06016559	A	19940125	JP 1993-81953	
19930408 <--				
JP 2613352	B2	19970528		

AT 161723 T 19980115 AT 1993-302780
19930408 <--
ES 2112386 T3 19980401 ES 1993-302780
19930408 <--
PRAI JP 1992-87115 A 19920408 <--
IT 141807-86-5P 141807-94-5P 141807-96-7P 141807-97-8P
141807-98-9P 142665-35-8P 142665-36-9P 142665-38-1P
147700-41-2P
147700-43-4P 147700-44-5P 147700-45-6P 147700-46-7P
147700-47-8P
147700-51-4P 147700-52-5P 147700-53-6P 147700-54-7P
151539-17-2P
151539-19-4P 151539-20-7P 151539-21-8P 151539-22-9P
151539-23-0P
151539-24-1P 151539-26-3P 151539-27-4P 151539-28-5P
151539-29-6P
151539-30-9P 151539-31-0P 151539-32-1P 151539-33-2P
151539-34-3P
151539-35-4P 151539-36-5P 151539-37-6P 151539-39-8P
151539-40-1P
151539-41-2P 151539-42-3P 151539-43-4P 151539-44-5P
151539-45-6P
151539-46-7P 151539-47-8P 151539-48-9P 151539-50-3P
151539-51-4P
151539-53-6P 151539-54-7P 151539-56-9P 151539-57-0P
151539-58-1P
151539-60-5P 151539-61-6P 151539-62-7P 151539-63-8P
151539-65-0P
151539-68-3P
RL: PREP (Preparation)
(preparation of, pharmaceutical composition containing, for
treatment of Parkinson's
disease)

L21 ANSWER 39 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:124633 CAPLUS Full-text
DOCUMENT NUMBER: 120:124633
ORIGINAL REFERENCE NO.: 120:21765a,21768a
TITLE: Photoisomerization of a potent and selective
adenosine
A2 antagonist,
(E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-
methylxanthine
AUTHOR(S): Nonaka, Yoshiko; Shimada, Junichi; Nonaka,
Hiromi;
Koike, Nobuaki; Aoki, Noboru; Kobayashi,
Hiroyuki;
Kase, Hiroshi; Yamaguchi, Kazuo; Suzuki, Fumio
CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd.,
Nagaizumi, 411, Japan
SOURCE: Journal of Medicinal Chemistry (1993),
36(23), 3731-3
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, E
II, Z

AB 1,3,7-Trialkylxanthines with (E)-8-styryl substituents are selective adenosine A2 receptor antagonists. The photoisomerization and binding affinity of (E)- (I) and (Z)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7- methylxanthines (II) have been examined Compound I was isomerized to its Z-isomer II under photo illumination by fluorescent light (1000 lx) in DMSO or methanol. Its photoisomerization was slow at high concentration (10 mM) of substrate but was fast at low concentration (0.1 mM) and an equilibrium mixture (82% Z-18%E) was eventually formed. This finding was substantiated by similarly exposing the Z-isomer II (0.1 mM) and obtaining the same equilibrium mixture The E-isomer I possesses potent affinity (Ki = 1.0 nM, Ki ratio of A1/A2 = 62) at the A2 receptor that is 800-fold higher than its Z-isomer II. Then the authors examined possibility of the E-Z isomerization in animals. Plasma and brain concns. of I 4 h after its oral administration in rats at a dose of 30 mg/kg, were 0.065 μg/mL and 0.076 μg/g brain, resp. None of the Z-isomer II was detected in plasma and brain. Although these concns. of I indicate poor oral bioavailability, they are sufficient to fully antagonize adenosine receptors in the heart and the CNS. Thus, compound I might be a useful pharmacol. probe in vivo for elucidating the physiol. and pathophysiol. roles of the A2 receptor.

TI Photoisomerization of a potent and selective adenosine A2 antagonist,
(E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthine

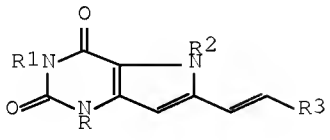
SO Journal of Medicinal Chemistry (1993), 36(23), 3731-3
CODEN: JMCMAR; ISSN: 0022-2623

IT 141807-96-7
RL: BIOL (Biological study)
(adenosinergic A2 antagonist activity and photoisomerization of)

L21 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:254617 CAPLUS Full-text
DOCUMENT NUMBER: 118:254617
ORIGINAL REFERENCE NO.: 118:44233a,44236a
TITLE: Structure-activity relationships of 8-styrylxanthines
as A2-selective adenosine antagonists
AUTHOR(S): Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Melman,
Neli; Fischer, Bilha; Maillard, Michel; van Bergen,
Andrew; van Galen, Philip J. M.; Karton, Yishai
CORPORATE SOURCE: Lab. Bioorg. Chem., Natl. Inst. Diabet.,

Digest.

Kidney Dis., Bethesda, MD, 20892, USA
SOURCE: Journal of Medicinal Chemistry (1993), 36(10), 1333-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of substituted 8-styryl derivs. of 1,3,7-alkylxanthines I [i.e., R-R2 = H, Me, R3 = (un)substituted Ph]was synthesized as potential A2-selective adenosine receptor antagonists, and the potency at rat brain A1- and A2-receptors was studied in radioligand binding expts. At the xanthine 7-position, only small hydrophobic substituents were tolerated in receptor binding. 7-Me analogs were roughly 1 order of magnitude more selective for A2 vs. A1 receptors than the corresponding 7-H analogs. 1,3-Dimethylxanthine derivs. tended to be more selective for A2-receptors than the corresponding 1,3-diallyl, di-Et, or di-Pr derivs. Substitutions of the Ph ring at the 3-(monosubstituted) and 3,5-(disubstituted) positions were favored. I (R - R2 = Me, R3 = 3-ClC6H4) was a moderately potent and high A2-selective adenosine antagonist. I (R - R2 = Me, R3 = 3-HO2CCH2CH2CONHC6H4) was highly A2-selective and had enhanced water solubility I [R, R1 = Pr, R2 = Me, R3 = 3,5-(MeO)2C6H3] was a potent and very A2-selective adenosine antagonist.

TI Structure-activity relationships of 8-styrylxanthines as A2-selective adenosine antagonists

SO Journal of Medicinal Chemistry (1993), 36(10), 1333-42
CODEN: JMCMAR; ISSN: 0022-2623

IT 51369-37-8P 99765-13-6P 132940-42-2P 141807-95-6P
141807-96-7P 142665-36-9P 147699-92-1P 147699-93-2P
147699-94-3P 147699-95-4P 147699-96-5P 147699-97-6P
147699-98-7P
147699-99-8P 147700-00-3P 147700-01-4P 147700-02-5P
147700-03-6P
147700-04-7P 147700-05-8P 147700-06-9P 147700-07-0P
147700-08-1P
147700-09-2P 147700-10-5P 147700-11-6P 147700-12-7P
147700-13-8P
147700-14-9P 147700-15-0P 147700-16-1P 147700-17-2P
147700-18-3P
147700-19-4P 147700-20-7P 147700-21-8P 147700-22-9P
147700-23-0P
147700-24-1P 147700-25-2P 147700-26-3P 147700-27-4P

147700-28-5P
147700-29-6P 147700-30-9P 147700-31-0P 147700-32-1P
147700-33-2P
147700-34-3P 147700-35-4P 147700-36-5P 147700-37-6P
147700-38-7P
147700-39-8P 147700-40-1P 147700-41-2P 147700-42-3P
147700-43-4P
147700-44-5P 147700-45-6P 147700-46-7P 147700-47-8P
147700-48-9P
147700-49-0P 147700-50-3P 147700-51-4P 147700-52-5P
147700-53-6P
147700-54-7P 147700-55-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and A2-selective adenosine antagonistic activity
of)

L21 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:490312 CAPLUS Full-text
DOCUMENT NUMBER: 117:90312
ORIGINAL REFERENCE NO.: 117:15773a,15776a
TITLE: Preparation of xanthine derivatives as
antiasthmatics
and agents for treating osteoporosis
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ishii, Akio;
Nonaka,
Hiromi; Kosaka, Nobuo; Ichikawa, Shunji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9206976	A1	19920430	WO 1991-JP1420	19911017 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2094270	A1	19920419	CA 1991-2094270	19911017 <--
CA 2094270	C	19970121		
EP 559893	A1	19930915	EP 1991-917824	19911017 <--
EP 559893	B1	19990203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 2843671	B2	19990106	JP 1991-516529	19911017 <--
AT 176470	T	19990215	AT 1991-917824	19911017 <--
ES 2130138	T3	19990701	ES 1991-917824	19911017 <--
US 5756735	A	19980526	US 1995-483159	19950607 <--
PRIORITY APPLN. INFO.:			JP 1990-280171	A

19901018 <--

WO 1991-JP1420 W

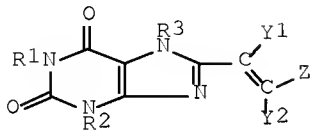
19911017 <--

US 1993-39193 B1

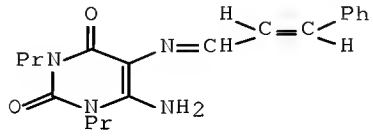
19930414 <--

OTHER SOURCE(S): CASREACT 117:90312; MARPAT 117:90312

GI



I



II

AB Xanthine derivs. [I, R1, R2 = H, Pr, Bu, allyl; R3 = H, alkyl; Y1, Y2 = H, Me, Z = (substituted) Ph, pyridyl, imidazolyl, furyl, thienyl], effective adenosine antagonists, are prepared and formulated. Condensation reaction of cinnamaldehyde with 5,6-diamino-1,3-dipropyluracil in MeOH-HOAc gave 70% enamine II, which was refluxed with FeCl3 in EtOH to give 61% (E)-I (R1 = R2 = Pr, R3 = Y2 = Y2 = H, Z = Ph) (III). Methylation of III with MeI in DMF gave 84% (E)-I (R3 = Me, others remain unchanged) which showed 82% inhibition of adenosine A1 receptor and 96% inhibition of A2 receptor at 10-4 M. I also showed 119% inhibition of bone absorption.

TI Preparation of xanthine derivatives as antiasthmatics and agents for treating osteoporosis

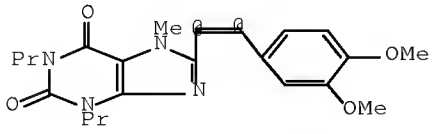
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI WO 9206976 A1 19920430

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9206976	A1	19920430	WO 1991-JP1420	19911017 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2094270	A1	19920419	CA 1991-2094270	19911017 <--
CA 2094270	C	19970121		
EP 559893	A1	19930915	EP 1991-917824	19911017 <--
EP 559893	B1	19990203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 2843671	B2	19990106	JP 1991-516529	19911017 <--
AT 176470	T	19990215	AT 1991-917824	

19911017 <--
ES 2130138 T3 19990701 ES 1991-917824
19911017 <--
US 5756735 A 19980526 US 1995-483159
19950607 <--
PRAI JP 1990-280171 A 19901018 <--
WO 1991-JP1420 W 19911017 <--
US 1993-39193 B1 19930414 <--
IT 141807-86-5P 141807-87-6P 141807-88-7P 141807-93-4P
141807-94-5P
141807-95-6P 141807-96-7P 141807-97-8P 141807-98-9P
141807-99-0P 141808-00-6P 141808-01-7P 141824-01-3P
142665-27-8P
142665-28-9P 142665-29-0P 142665-30-3P 142665-31-4P
142665-32-5P
142665-33-6P 142665-34-7P 142665-35-8P 142665-36-9P
142665-37-0P
142665-38-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiasthmatic and antiosteoporosis agent)

L21 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:419919 CAPLUS Full-text
DOCUMENT NUMBER: 117:19919
ORIGINAL REFERENCE NO.: 117:3417a,3420a
TITLE: (E)-1,3-Dialkyl-7-methyl-8-(3,4,5-trimethoxystyryl)xanthines: potent and selective adenosine A2 antagonists
AUTHOR(S): Shimada, Junichi; Suzuki, Fumio; Nonaka, Hiromi; Ishii, Akio; Ichikawa, Shunji
CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Nagaizumicho, Japan
SOURCE: Journal of Medicinal Chemistry (1992), 35(12), 2342-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of 8-substituted 1,3,7-trialkylxanthines was tested for their hydrophobic interactions with the adenosine A2 receptor. (E)-Styryl substitution at the 8-position increased the affinity at the A2 receptor and A2 selectivity. Furthermore introduction of dimethoxy or trimethoxy group into the 8-styryl substituent of

1,3-dipropyl-7-methylxanthines enhanced the A2 selectivity in general. No apparent differences in the affinity at the A2 receptor were observed among a series of (E)-1,3-dialkyl-7-methyl-8-(3,5,6-trimethoxystyryl)xanthine derivs. This result is greatly contrasting with that of 1,3-disubstituted 8-alkyl- or 8-polycycloalkylxanthine derivs. where 1,3-disubstituents dramatically influenced affinity at the A1 receptor and its selectivity. The most potent A2 antagonist, (E)-1,3-dipropyl-7-methyl-8-(3,4- dimethoxystyryl)xanthine (I) (Ki = 7.8 nM, A1/A2 = 190) produced a much larger shift of the NECA dose-response curve for blood pressure (A2) than for heart rate (A1) at the oral dose of 30 mg/kg.

TI (E)-1,3-Dialkyl-7-methyl-8-(3,4,5-trimethoxystyryl)xanthines: potent and selective adenosine A2 antagonists

SO Journal of Medicinal Chemistry (1992), 35(12), 2342-5
CODEN: JMCMAR; ISSN: 0022-2623

IT 120362-53-0 132940-39-7 132940-42-2 141807-86-5 141807-87-6
141807-88-7 141807-89-8 141807-90-1 141807-91-2 141807-92-3
141807-93-4 141807-94-5 141807-95-6 141807-96-7
141807-97-8 141807-98-9 141807-99-0 141808-00-6 141808-01-7
141824-00-2 141824-01-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine A2 receptor antagonist activity of)

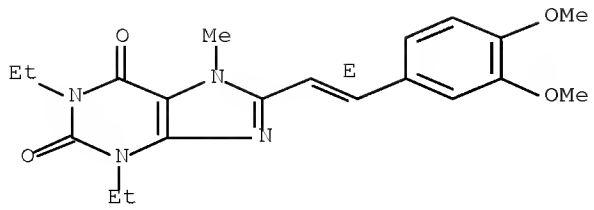
L21 ANSWER 43 OF 43 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1974:40984 CAPLUS Full-text
DOCUMENT NUMBER: 80:40984
ORIGINAL REFERENCE NO.: 80:6687a,6690a
TITLE: Photo-induced isomerization of 8-(3,4,5-trimethoxystyryl)caffeine as possible route of drug decomposition
AUTHOR(S): Philip, Jose; Szulczewski, Dale H.
CORPORATE SOURCE: Pharm. Res. Dev. Dep., Parke, Davis and Co., Detroit, MI, USA
SOURCE: Journal of Pharmaceutical Sciences (1973), 62(11), 1885-7
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English

AB trans-8-(3,4,5-Trimethoxystyryl)caffeine, dissolved in MeOH or CHCl3 rapidly isomerizes to an equilibrium mixture of trans-cis-isomers in the presence of visible light. Geometric isomerization was estimated by catalytic hydrogenation of both reactant and product to yield 8-(3,4,5-trimethoxyphenethyl)caffeine.

TI Photo-induced isomerization of 8-(3,4,5-trimethoxystyryl)caffeine as possible route of drug decomposition

SO Journal of Pharmaceutical Sciences (1973), 62(11), 1885-7
CODEN: JPMSAE; ISSN: 0022-3549

```
IT   51369-37-8
     RL: PROC (Process)
        (photoisomerization of)

http://www.cas.org/support/stngen/stndoc/properties.html

=> e 155270-99-8/rn
E1            1     155270-97-6/RN
E2            1     155270-98-7/RN
E3            1 --> 155270-99-8/RN
E4            1     155271-00-4/RN
E5            1     155271-01-5/RN
E6            1     155271-02-6/RN
E7            1     155271-03-7/RN
E8            1     155271-04-8/RN
E9            1     155271-05-9/RN
E10           1     155271-06-0/RN
E11           1     155271-07-1/RN
E12           1     155271-08-2/RN

=> set expand continuous
SET COMMAND COMPLETED

=> s e3
L7            1 155270-99-8/RN

=> d l7

L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
     dihydro-7-methyl-, (E)-
OTHER NAMES:
CN   Istradefylline
CN   KW 6002
FS   STEREOSEARCH
MF   C20 H24 N4 O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
CA,
       CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS,
IMSRESEARCH,
       IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE,
TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Double bond geometry as shown.
```



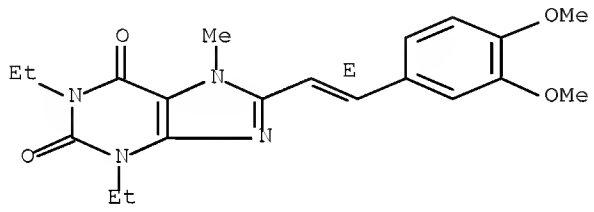
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e istradefylline/cn
E13          1     ISTONIL/CN
E14          1     ISTOPIRIN/CN
E15          1 --> ISTRADEFYLLINE/CN
E16          1     ISTROEKOL/CN
E17          1     ISTRONA/CN
E18          1     ISU-CCUR/CN
E19          1     ISUBGOL/CN
E20          1     ISUHUMAN/CN
E21          1     ISUMELINE/CN
E22          1     ISUPREL/CN
E23          1     ISUPREN/CN
E24          1     ISURETIN/CN

=> s e15
L8           1 ISTRADEFYLLINE/CN

=> d l8

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-3,7-
     dihydro-7-methyl-, (E)-
OTHER NAMES:
CN   Istradefylline
CN   KW 6002
FS   STEREOSEARCH
MF   C20 H24 N4 O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO,
```

CA,
CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



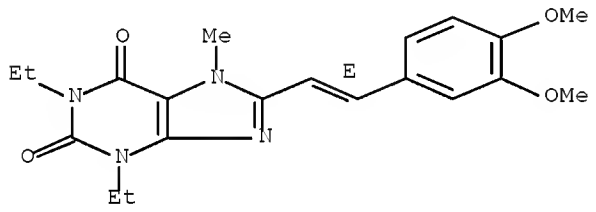
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

103 REFERENCES IN FILE CA (1907 TO DATE)
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> e kw 6002/cn
E25             1     KW 6/CN
E26             2     KW 600/CN
E27             1 --> KW 6002/CN
E28             1     KW 600S/CN
E29             1     KW 6055/CN
E30             1     KW 6066N/CN
E31             1     KW 6151/CN
E32             1     KW 622/CN
E33             1     KW 6629/CN
E34             1     KW 677/CN
E35             1     KW 678/CN
E36             1     KW 7/CN

=> s e27
L9              1 "KW 6002"/CN

=> d l9

L9   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   155270-99-8  REGISTRY
ED   Entered STN:  24 May 1994
CN   1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
diethyl-
     3,7-dihydro-7-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-
```

diethyl-3,7-
dihydro-7-methyl-, (E)-
OTHER NAMES:
CN Istradefylline
CN KW 6002
FS STEREOSEARCH
MF C20 H24 N4 O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,
CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH,
IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s (l7 or l8 or l9)
           104 L7
           104 L8
           104 L9
L10        104 (L7 OR L8 OR L9)

=> s l10 and adenosin?
        101764 ADENOSIN?
L11         85 L10 AND ADENOSIN?

=> s l11 and antagonist?
        272342 ANTAGONIST?
L12         82 L11 AND ANTAGONIST?

=> s l12 and (py<2003 or ay<2003 or pry<2003)
      22983605 PY<2003
       4504987 AY<2003
       3974028 PRY<2003
L13         28 L12 AND (PY<2003 OR AY<2003 OR PRY<2003)
```

=> d l13 ibib abs ti hit 1-5

L13 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:579608 CAPLUS Full-text
DOCUMENT NUMBER: 145:40296
TITLE: Adenosine A2a receptor antagonists for the treatment of extra-pyramidal syndrome and other movement disorders
INVENTOR(S): Grzelak, Michael; Hunter, John; Pond, Annamarie; Varty, Geoffrey
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 234,644.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060128694	A1	20060615	US 2005-249796	20051013 <--
US 20040138235	A1	20040715	US 2003-738906	20031217 <--
US 7414058	B2	20080819		
CA 2510655	A1	20050519	CA 2003-2510655	20031217 <--
AU 2003304527	A1	20050526	AU 2003-304527	20031217 <--
EP 1578409	A1	20050928	EP 2003-818838	20031217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017436	A	20051116	BR 2003-17436	20031217 <--
JP 2006514697	T	20060511	JP 2005-510511	20031217 <--
NZ 540493	A	20080430	NZ 2003-540493	20031217 <--
CN 101310724	A	20081126	CN 2008-10136154	20031217 <--
MX 2005006790	A	20050908	MX 2005-6790	20050620 <--
US 20060106040	A1	20060518	US 2005-234644	20050923 <--
AU 2006304102	A1	20070426	AU 2006-304102	20061011
CA 2625859	A1	20070426	CA 2006-2625859	20061011
WO 2007047293	A1	20070426	WO 2006-US39689	20061011

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 2001511 A1 20081217 EP 2006-825743 20061011

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

MX 2008004876 A 20080625 MX 2008-4876 20080414

NO 2008002175 A 20080711 NO 2008-2175 20080509

CN 101325974 A 20081217 CN 2006-80046347 20080610

PRIORITY APPLN. INFO.: US 2002-435321P P 20021219 <--

US 2003-738906 A2 20031217

US 2005-234644 A2 20050923

CN 2003-80107087 A3 20031217

WO 2003-US40456 W 20031217

US 2005-249796 A 20051013

WO 2006-US39689 W 20061011

OTHER SOURCE(S): MARPAT 145:40296

AB A method for the treatment or prevention of extra pyramidal syndrome (EPS), dystonia, restless legs syndrome (RLS) or periodic leg movement in sleep (PLMS) comprising the administration of an adenosine A2a receptor antagonist, alone or in combination with other agents is described. Pharmaceutical compns. consisting of an adenosine A2a receptor antagonist in combination with an antipsychotic agent, an anticonvulsant agent, lithium or an opioid

are also provided. Thus, monkeys, previously sensitized to the chronic effects of haloperidol, that exhibited EPS when administered haloperidol acutely, were used in a crossover, balanced design study to evaluate adenosine A2a receptor antagonist administered orally, in conjunction with haloperidol. The adenosine A2a receptor antagonist studied prevented the onset of EPS and delayed the onset of EPS by an average of 2.3 to 2.9 h.

TI Adenosine A2a receptor antagonists for the treatment of extra-pyramidal syndrome and other movement disorders

TI Adenosine A2a receptor antagonists for the treatment of extra-pyramidal syndrome and other movement disorders

L13 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:463565 CAPLUS Full-text
DOCUMENT NUMBER: 144:460860
TITLE: Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders
INVENTOR(S): Grzelak, Michael; Hunter, John; Pond, Annamarie; Varty, Geoffrey
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 738,906.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060106040	A1	20060518	US 2005-234644	20050923 <--
US 20040138235	A1	20040715	US 2003-738906	20031217 <--
US 7414058	B2	20080819		
CA 2510655	A1	20050519	CA 2003-2510655	20031217 <--
AU 2003304527	A1	20050526	AU 2003-304527	20031217 <--
EP 1578409	A1	20050928	EP 2003-818838	20031217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017436	A	20051116	BR 2003-17436	20031217 <--
JP 2006514697	T	20060511	JP 2005-510511	20031217 <--
NZ 540493	A	20080430	NZ 2003-540493	20031217 <--

CN 101310724 A 20081126 CN 2008-10136154
20031217 <--
MX 2005006790 A 20050908 MX 2005-6790
20050620 <--
US 20060128694 A1 20060615 US 2005-249796
20051013 <--
AU 2006294919 A1 20070405 AU 2006-294919
20060921
CA 2623040 A1 20070405 CA 2006-2623040
20060921
WO 2007038212 A1 20070405 WO 2006-US36864
20060921
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG,
MK, MN,
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR,
TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,
BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,
BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY,
KG, KZ, MD, RU, TJ, TM
EP 1940408 A1 20080709 EP 2006-815125
20060921
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK,
TR, AL,
BA, HR, MK, RS
JP 2009508967 T 20090305 JP 2008-532393
20060921
MX 2008004006 A 20080410 MX 2008-4006
20080324
CN 101312731 A 20081126 CN 2006-80043146
20080519
PRIORITY APPLN. INFO.: US 2002-435321P P
20021219 <--
US 2003-738906 A2
20031217
CN 2003-80107087 A3
20031217
WO 2003-US40456 W
20031217
US 2005-234644 A2
20050923

WO 2006-US36864 W 20060921
OTHER SOURCE(S): MARPAT 144:460860
AB The invention discloses a method for the treatment or prevention of extrapyramidal syndrome (EPS), dystonia, restless legs syndrome (RLS) or periodic leg movement in sleep (PLMS), comprising the administration of an adenosine A2a receptor antagonist, alone or in combination with other agents useful for treating EPS, dystonia, RLS or PLMS.
TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders
TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders

L13 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:203674 CAPLUS Full-text
DOCUMENT NUMBER: 140:229467
TITLE: Adenosine A2A receptor antagonists for treating restless legs syndrome or related disorders
INVENTOR(S): Kase, Hiroshi; Seno, Naoki; Mori, Akihisa; Zhao, Dayao
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co. Ltd., Japan
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019949	A1	20040311	WO 2003-US26644	20030827 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2496920	A1	20040311	CA 2003-2496920	20030827 <--
AU 2003262860	A1	20040319	AU 2003-262860	

20030827 <--
EP 1534289 A1 20050601 EP 2003-791769
20030827 <--
EP 1534289 B1 20080709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003013503 A 20050621 BR 2003-13503
20030827 <--
CN 1671390 A 20050921 CN 2003-818000
20030827 <--
JP 2005539050 T 20051222 JP 2004-533000
20030827 <--
AT 400275 T 20080715 AT 2003-791769
20030827 <--
ES 2310258 T3 20090101 ES 2003-791769
20030827 <--
MX 2005001461 A 20050603 MX 2005-1461
20050204 <--
US 20050245545 A1 20051103 US 2005-523603
20050204 <--
PRIORITY APPLN. INFO.: US 2002-406955P P
20020830 <--
WO 2003-US26644 W
20030827
OTHER SOURCE(S): MARPAT 140:229467
AB The invention provides methods of treating restless legs syndrome or related disorders, comprising administering an effective amount of at least one adenosine A2A receptor antagonist to a patient in need thereof. More preferably the adenosine A2A receptor antagonist is a xanthine derivative or a pharmaceutically acceptable salt thereof.
TI Adenosine A2A receptor antagonists for treating restless legs syndrome or related disorders

L13 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:610271 CAPLUS Full-text
DOCUMENT NUMBER: 139:143978
TITLE: Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine agonist therapy-associated movement disorders
INVENTOR(S): Kase, Hiroshi; Mori, Akihisa; Waki, Yutaka; Ohsawa, Yutaka; Karasawa, Akira; Kuwana, Yoshitoshi
PATENT ASSIGNEE(S): Japan
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

```
----
     WO 2003063876         A2    20030807    WO 2003-US2658
20030128 <--
     WO 2003063876         A3    20031127
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK,
LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM,
PH, PL,
             PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA,
             UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK,
TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2473864            A1    20030807    CA 2003-2473864
20030128 <--
     US 20040198753        A1    20041007    US 2003-353240
20030128 <--
     EP 1469855            A2    20041027    EP 2003-705971
20030128 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003006919         A     20041109    BR 2003-6919
20030128 <--
     CN 1646132            A     20050727    CN 2003-802847
20030128 <--
     JP 2005523898         T     20050811    JP 2003-563566
20030128 <--
     AU 2003207734         B2    20080221    AU 2003-207734
20030128 <--
     MX 2004007299         A     20041029    MX 2004-7299
20040728 <--
     US 20060148827        A1    20060706    US 2006-326516
20060106 <--
     US 20060178379        A1    20060810    US 2006-326414
20060106 <--
     AU 2008200611         A1    20080306    AU 2008-200611
20080208
PRIORITY APPLN. INFO.:                         US 2002-352413P     P
20020128 <--
                                               AU 2003-207734      A3
20030128
                                               US 2003-353240      A3
20030128
                                               WO 2003-US2658      W
20030128
OTHER SOURCE(S):         MARPAT 139:143978
```

AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e., L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.

TI Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine agonist therapy-associated movement disorders

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine agonist therapy-associated movement disorders

PRAI US 2002-352413P P 20020128 <--
AU 2003-207734 A3 20030128
US 2003-353240 A3 20030128
WO 2003-US2658 W 20030128

AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e., L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.

ST DOPA motor complication Parkinson drug adenosine A2a antagonist; dopamine agonist motor complication Parkinson drug adenosine A2a antagonist

IT Purinoceptor antagonists
(A2; adenosine A2a antagonist for treating
Parkinson's disease patients with L-DOPA/dopamine agonist
therapy-associated motor complications)
IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2A; adenosine A2a antagonist for treating
Parkinson's disease patients with L-DOPA/dopamine agonist
therapy-associated motor complications)

L13 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:472597 CAPLUS Full-text
DOCUMENT NUMBER: 139:47145
TITLE: Methods for using extracellular adenosine inhibitors and adenosine receptor inhibitors to enhance immune response and inflammation
INVENTOR(S): Sitkovsky, Michail V.; Ohta, Akio
PATENT ASSIGNEE(S): The Government of the United States of America as
Represented by the Secretary, Department of Health and
Human Services, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050241	A2	20030619	WO 2002-US36829	20021114 <--
WO 2003050241	A3	20040129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2470104	A1	20030619	CA 2002-2470104	20021114 <--

AU 2002356962 A1 20030623 AU 2002-356962
20021114 <--
EP 1465634 A2 20041013 EP 2002-804693
20021114 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
JP 2005516917 T 20050609 JP 2003-551263
20021114 <--
US 20050220799 A1 20051006 US 2004-498416
20040610 <--
PRIORITY APPLN. INFO.: US 2001-340772P P
20011212 <--
US 2001-342585P P
20011219 <--
WO 2002-US36829 W
20021114 <--

AB A method is provided to increase an immune response to an antigen. The method includes administering an agent that inhibits extracellular adenosine or inhibits adenosine receptors. Also disclosed are methods to increase the efficacy of a vaccine and to increase an immune response to a tumor antigen or immune cell-mediated tumor destruction.

TI Methods for using extracellular adenosine inhibitors and adenosine receptor inhibitors to enhance immune response and inflammation

=> d l13 ibib abs ti hit 6-15

L13 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:135720 CAPLUS Full-text
DOCUMENT NUMBER: 139:239332
TITLE: Adenosine A↓2↓A receptor antagonists-A novel approach to therapeutic drug for parkinsonism
AUTHOR(S): Kase, Hiroshi
CORPORATE SOURCE: Kyowa Hakko Kogyo Co., Ltd., Tokyo, Chiyoda, Ohtemachi, 100-8185, Japan
SOURCE: Seitai no Kagaku (2002), 53(6), 592-600
CODEN: SEKAA6; ISSN: 0370-9531
PUBLISHER: Kanehara Ichiro Kinen Igaku Iryo Shinko Zaidan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review, discussing the action mechanism and clin. pharmacol. of adenosine A↓2↓A receptor antagonists, including KW 6002 for treatment of parkinsonism.

TI Adenosine A↓2↓A receptor antagonists-A novel approach to therapeutic drug for parkinsonism

TI Adenosine A↓2↓A receptor antagonists-A novel approach to therapeutic drug for parkinsonism

SO Seitai no Kagaku (2002), 53(6), 592-600
CODEN: SEKAA6; ISSN: 0370-9531

AB A review, discussing the action mechanism and clin. pharmacol. of adenosine A↓2↓A receptor antagonists, including KW 6002 for treatment of parkinsonism.

ST review adenosine A2A receptor antagonists

antagonist parkinsonism
IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2; adenosine A↓2↓A receptor
antagonists-A novel approach to therapeutic drug for
parkinsonism)
IT Antiparkinsonian agents
Human
Parkinson's disease
(adenosine A↓2↓A receptor antagonists
-A novel approach to therapeutic drug for parkinsonism)
IT 155270-99-8, KW 6002
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(adenosine A↓2↓A receptor antagonists
-A novel approach to therapeutic drug for parkinsonism)

L13 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:793451 CAPLUS Full-text
DOCUMENT NUMBER: 137:289033
TITLE: Adenosine A2A receptor antagonists
combined with neurotrophic activity compounds
in the
treatment of Parkinson's disease
INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen,
Karin
Sandager
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080957	A1	20021017	WO 2002-DK228	20020404 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,

TD, TG
CA 2440196 A1 20021017 CA 2002-2440196
20020404 <--
AU 2002338309 A1 20021021 AU 2002-338309
20020404 <--
EP 1379269 A1 20040114 EP 2002-759761
20020404 <--
EP 1379269 B1 20090304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004529916 T 20040930 JP 2002-578996
20020404 <--
US 20040097540 A1 20040520 US 2003-473809
20031002 <--
US 7160899 B2 20070109
MX 2003009185 A 20040217 MX 2003-9185
20031008 <--
PRIORITY APPLN. INFO.: DK 2001-583 A
20010409 <--
WO 2002-DK228 W
20020404 <--
AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H- pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublastin; and pharmaceutically acceptable salts thereof.
TI Adenosine A2A receptor antagonists combined with neurotrophic activity compounds in the treatment of Parkinson's disease
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Adenosine A2A receptor antagonists combined with neurotrophic activity compounds in the treatment of Parkinson's disease
PI WO 2002080957 A1 20021017
PATENT NO. KIND DATE APPLICATION NO. DATE
---------- ---- -------- ---------- ----
PI WO 2002080957 A1 20021017 WO 2002-DK228
20020404 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2440196 A1 20021017 CA 2002-2440196 20020404 <--
AU 2002338309 A1 20021021 AU 2002-338309 20020404 <--
EP 1379269 A1 20040114 EP 2002-759761 20020404 <--
EP 1379269 B1 20090304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004529916 T 20040930 JP 2002-578996 20020404 <--
US 20040097540 A1 20040520 US 2003-473809 20031002 <--
US 7160899 B2 20070109
MX 2003009185 A 20040217 MX 2003-9185 20031008 <--
PRAI DK 2001-583 A 20010409 <--
WO 2002-DK228 W 20020404 <--

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H- pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublastin; and pharmaceutically acceptable salts thereof.

ST adenosine receptor antagonist neurotrophic Parkinson disease antiparkinsonian

IT Purinoceptor antagonists
(A2; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

L13 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:787693 CAPLUS Full-text
DOCUMENT NUMBER: 138:314421
TITLE: Distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in the rat brain
AUTHOR(S): Aoyama, Shiro; Koga, Kumiko; Mori, Akihisa; Miyaji,
Hiromasa; Sekine, Susumu; Kase, Hiroshi; Uchimura,

Tatsuo; Kobayashi, Hiroyuki; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Res. Inst., Kyowa Hakko Kogyo Co. Ltd.,
Sunto-gun, Shizuoka, 411-8731, Japan
SOURCE: Brain Research (2002), 953(1,2), 119-125
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione], possesses antiparkinsonian activities in rodent and primate models. In the present study, the authors investigated the distribution of [14C]KW-6002 in forebrain after oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [14C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the brain. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [14C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-containing neurons but not striatonigral substance P-containing neurons.
TI Distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in the rat brain

L13 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:90903 CAPLUS Full-text
DOCUMENT NUMBER: 136:277364
TITLE: Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease
AUTHOR(S): Ikeda, Ken; Kurokawa, Masako; Aoyama, Shiro; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411-8731, Japan
SOURCE: Journal of Neurochemistry (2002), 80(2), 262-270
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenosine A2A receptors are abundant in the caudate-putamen and involved in the motor control in several species. In MPTP-treated monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the present study, a significant neuroprotective effect of A2A receptor antagonists is shown in exptl. models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The neuroprotective property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically neuroprotective activities.

TI Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease

L13 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:943 CAPLUS Full-text
DOCUMENT NUMBER: 137:88308
TITLE: Adenosine A2A receptor antagonists : Potential therapeutic and neuroprotective effects in Parkinson's disease
AUTHOR(S): Morelli, M.; Wardas, J.
CORPORATE SOURCE: Department of Toxicology, University of Cagliari, Palazzo delle Scienze, Cagliari, 09124, Italy
SOURCE: Neurotoxicity Research (2001), 3(6), 545-556
CODEN: NURRFI; ISSN: 1029-8428
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The most effective treatment of Parkinson's disease (PD) is, at present, the dopamine precursor L-3,4-dihydroxyphenyl-alanine (L-DOPA), however a number of disadvantages such as a loss of drug efficacy and severe side-effects (psychoses, dyskinesias and on-off phenomena) limit long-term, effective utilization of this drug. Recent exptl. studies in which selective antagonists of adenosine A2A receptors were used, have shown an improvement in motor disabilities in animal models of PD. The A2A antagonist

[7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-(4,3-e)-1,2,4-triazolo(1,5- -c)pyrimidine] (SCH 58261) potentiated the contralateral turning behavior induced by a threshold dose of L-DOPA or direct dopamine receptor agonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, an effect accompanied by an increase in Foslike-immunoreactivity in neurons of the lesioned striatum. Likewise, other A2A receptor antagonists such as (3,7-dimethyl-1-propargylxanthine) (DMPX), [E-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] (KF 17837) and [E-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2, 6-dione] (KW 6002) antagonized catalepsy induced by haloperidol or reserpine in the rat, whereas in non-human primate models of PD, KW 6002 reduced the rigidity and improved the disability score of MPTP-treated marmosets and cynomolgus monkeys. Moreover, in contrast to L-DOPA, selective A2A receptor antagonists administered chronically did not produce dyskinesias and did not evoke tolerance in 6-OHDA and MPTP models of PD. An addnl. therapeutic potential of adenosine A2A antagonists emerged from studies showing neuroprotective properties of these compds. in animal models of cerebral ischemia and excitotoxicity, as well as in the (1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine) (MPTP) model of PD. Adenosine A2A receptor antagonists by reversing motor impairments in animal models of PD and by contrasting cell degeneration are some of the most promising compds. for the treatment of PD.

TI Adenosine A2A receptor antagonists: Potential therapeutic and neuroprotective effects in Parkinson's disease

L13 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:915602 CAPLUS Full-text

DOCUMENT NUMBER: 136:303408

TITLE: New developments in A1 and A2 adenosine receptor antagonists

AUTHOR(S): Kiec-Kononowicz, K.; Drabczynska, A.; Pekala, E.; Michalak, B.; Miller, C. E.; Schumacher, B.; Karolak-Wojciechowska, J.; Duddeck, H.; Rockitt, S.; Wartchow, R.

CORPORATE SOURCE: IUPAC Commission, Medical College, Department of Chemical Technology of Drugs, Jagiellonian University, Krakow, PL 30-688, Pol.

SOURCE: Pure and Applied Chemistry (2001), 73(9), 1411-1420
CODEN: PACHAS; ISSN: 0033-4545

PUBLISHER: International Union of Pure and Applied Chemistry

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with refs. The aim of this article is to briefly present progress in the development of the potent adenosine receptor (AR) antagonists with high selectivity for either A1, A2A or A2B ARs. The structural requirements for each AR subtype were discussed as well as their potential therapeutic use. In the search for new AR

antagonists. series of imidazo-, pyrimido-, and diazepino-purindione derivs. as well as oxazolo-, oxazino-, and oxazepino-purindiones were designed, synthesized, and preliminarily evaluated in pharmacol. studies. Oxygen-containing tricyclic derivs. were shown to be moderately potent AR antagonists exhibiting selectivity either for A1 or A2A ARs. Tricyclic purindiones with nitrogen in the third ring were generally more A2A AR selective. The compds. tested in vivo according to the Antiepileptic Drug Development Program of the National Institutes of Health (USA) were generally active as anticonvulsants in chemical induced seizures.

TI New developments in A1 and A2 adenosine receptor antagonists

L13 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:910700 CAPLUS Full-text

DOCUMENT NUMBER: 136:31603

TITLE: Neuroprotection by caffeine and A2A adenosine receptor inactivation in a model of Parkinson's disease

AUTHOR(S): Chen, Jiang-Fan; Xu, Kui; Petzer, Jacobus P.; Staal, Roland; Xu, Yue-Hang; Beilstein, Mark; Sonsalla, Patricia K.; Castagnoli, Kay; Castagnoli, Neal, Jr.; Schwarzschild, Michael A.

CORPORATE SOURCE: Molecular Neurobiology Laboratory, Department of Neurology, Massachusetts General Hospital, Charlestown, MA, 02129, USA

SOURCE: Journal of Neuroscience (2001), 21(10), RC143/1-RC143/6
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent epidemiol. studies have established an association between the common consumption of coffee or other caffeinated beverages and a reduced risk of developing Parkinson's disease (PD). To explore the possibility that caffeine helps prevent the dopaminergic deficits characteristic of PD, we investigated the effects of caffeine and the adenosine receptor subtypes through which it may act in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) neurotoxin model of PD. Caffeine, at doses comparable to those of typical human exposure, attenuated MPTP-induced loss of striatal dopamine and dopamine transporter binding sites. The effects of caffeine were mimicked by several A2A antagonists (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3- e]-1,2,4-triazolo[1,5-c]pyrimidine (SCH 58261), 3,7-dimethyl-1-propargyl xanthine, and (E)-1,3-diethyl-8 (KW-6002)-(3,4-dimethoxystyryl)-7-methyl- 3,7-dihydro-1H-purine-2,6-dione) (KW-6002) and by genetic inactivation of the A2A receptor, but not by A1 receptor blockade with 8-cyclopentyl-1,3-dipropylxanthine,

suggesting that caffeine attenuates MPTP toxicity by A2A receptor blockade. These data establish a potential neural basis for the inverse association of caffeine with the development of PD, and they enhance the potential of A2A antagonists as a novel treatment for this neurodegenerative disease.

TI Neuroprotection by caffeine and A2A adenosine receptor inactivation in a model of Parkinson's disease

L13 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:864519 CAPLUS Full-text
DOCUMENT NUMBER: 136:129190
TITLE: Solubilization and immunoprecipitation of rat striatal adenosine A2A receptors
AUTHOR(S): Harvey, Victoria; Jones, Julie; Misra, Anil; Knight, Antony R.; Quirk, Kathleen
CORPORATE SOURCE: Department of Molecular Pharmacology, Vernalis Research Ltd., Winnersh, Wokingham, RG41 5UA, UK
SOURCE: European Journal of Pharmacology (2001), 431(2), 171-177
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, the authors have sought to solubilize adenosine A2A receptors from rat striatal membranes using a variety of different detergents. Of the detergents tested, 1% CHAPS yielded optimal conditions for solubilization (in the presence of 3 mg/mL protein, 44% of receptor was solubilized, 50% of total protein was solubilized). An antipeptide antibody was raised against a 15 amino-acid sequence within the predicted third intracellular loop region of the human and rat adenosine A2A receptor. The antibody was coupled to protein A immobilized on sepharose CL-4B and used to immunoppt. adenosine A2A receptors from solubilized rat striatal prepns. Radioligand-binding studies were performed using the selective adenosine A2 antagonist [3H]ZM 241385. Using [3H]ZM 241385, the pharmacol. of immunopptd. adenosine A2A receptors was composed to striatal membrane bound adenosine A2A receptors and detergent solubilized adenosine A2A receptors. [H]ZM 241385 labeled a single saturable binding site with high affinity in all three prepns. (membrane bound Kd 2.7 nM; solubilized Kd 1.9 nM; immunopptd. Kd 2.2 nM). Addnl., all three assays confirmed a rank order of potency for displacers consistent with adenosine A2A receptor pharmacol.: ZM 241385 > KW 6002 > CGS 21680 > DPCPX. The authors conclude that they have solubilized and immunopptd. adenosine A2A receptors from rat striatum and that their pharmacol. is consistent with native striatal adenosine A2A receptors.

TI Solubilization and immunoprecipitation of rat striatal adenosine A2A receptors

L13 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:688889 CAPLUS Full-text
DOCUMENT NUMBER: 136:48351
TITLE: Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice
AUTHOR(S): El Yacoubi, Malika; Ledent, Catherine; Parmentier, Marc; Bertorelli, Rosalia; Ongini, Ennio; Costentin, Jean; Vaugeois, Jean-Marie
CORPORATE SOURCE: UMR 6036 CNRS, IFRMP 23, U.F.R. de Medecine and Pharmacie, Rouen, 76183, Fr.
SOURCE: British Journal of Pharmacology (2001), 134(1), 68-77
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenosine, an ubiquitous neuromodulator, and its analogs have been shown to produce "depressant" effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine -mediated "depressant" effect. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clin. antidepressant activity. Adenosine A2A receptor knockout mice were found to be less sensitive to "depressant" challenges than their wild-type littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1-10 mg kg-1, i.p.) and KW 6002 (0.1-10 mg kg-1, p.o.) reduced the total immobility time in the tail suspension test. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1-10 mg kg-1) and ZM 241385 (15-60 mg kg-1) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg-1 reduced immobility of mice that were selectively bred for their spontaneous "helplessness" in this assay. Addnl. expts. were carried out using the forced swim test. SCH 58261 at 10 mg kg-1 reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg-1 by 75 and 79%, resp. Administration of the dopamine D2 receptor antagonist haloperidol (50-200 μg kg-1 i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg-1 i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behavior in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

TI Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout

mice